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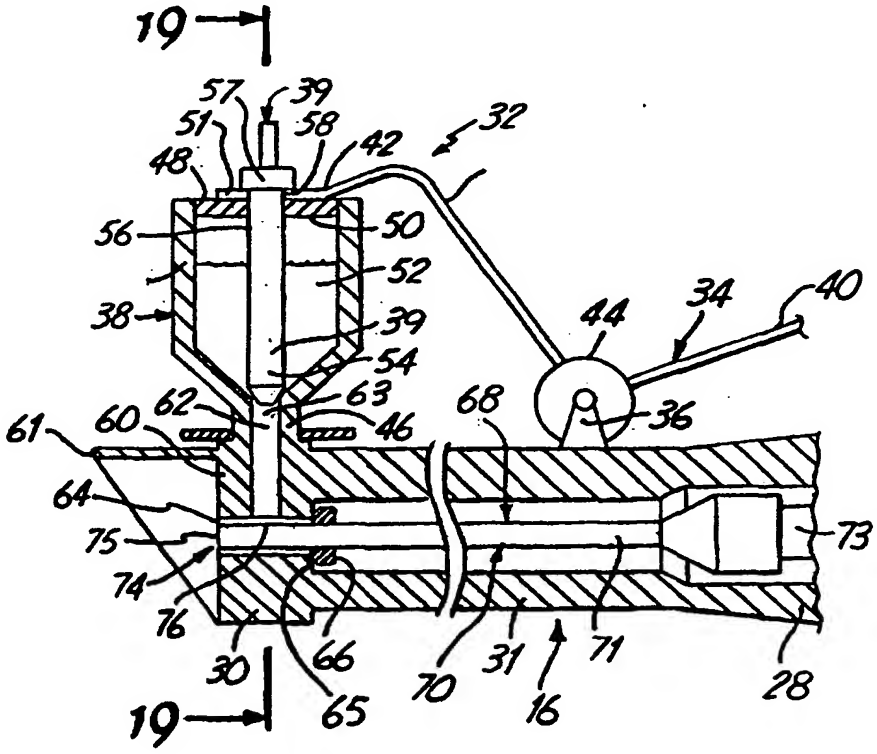
(54) Title: METHOD OF SPRAYING A SURFACE USING ULTRASONIC RADIATION

(57) Abstract

A method of spraying human tissue using an ultrasonic transducer (70) that produces low frequency ultrasonic waves. The transducer has a tip (74) with a free end (75) surface directly exposed to a surrounding environment. The spray is projected, and the particles of the spray provide a medium for transmission of the ultrasonic radiation emanating from the free end surface. The particle spray is oriented directly onto the surface to be sprayed while maintaining a distance of separation between the surface to be sprayed and the free end surface of the transducer.



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METHOD OF SPRAYING A SURFACE USING ULTRASONIC RADIATION

BACKGROUND OF THE INVENTION

The present invention relates to methods of using ultrasonic radiation in spraying applications. In particular, the present invention relates to a method of spraying a surface using ultrasonic radiation for delivering drugs, killing bacteria, and cleansing a surface.

Ultrasonic radiation has been widely used in medical applications including both diagnostics and therapy as well as many other non-medical applications. One diagnostic use of ultrasound radiation includes using ultrasonic radiation to detect underlying structures in an object or a human tissue. In this method, an ultrasonic transducer is placed in contact with the tissue (or object) via a coupling medium and high frequency ultrasonic waves (e.g., 1-3 Megahertz) are directed into the tissue (or object). Upon contact with the various underlying structures, the waves are reflected back to a receiver adjacent the transducer. By comparing the signals of the ultrasonic wave as sent with the reflected ultrasonic wave as received, an image of the underlying structure can be produced. This technique is particularly useful for identifying boundaries between components of tissue and can be used to detect irregular masses, e.g., tumors. This technique can also be used to detect the underlying structure of objects other than human or animal tissue.

Two therapeutic medical uses of ultrasound radiation include aerosol mist production and contact physiotherapy. Aerosol mist production makes use of a nebulizer to produce an aerosol mist for creating a humid environment. Ultrasonic nebulizers operate by passing a beam of ultrasound radiation of sufficient intensity through a liquid, the beam being directed at an air-liquid interface of the liquid from a point underneath or within the liquid. Liquid particles are ejected from the surface of the liquid into the surrounding air following the disintegration of capillary waves produced by the ultrasonic

radiation. This technique can produce a very fine dense fog or mist and typically is used within a tent or canopy for maintaining a humid atmosphere in a ventilating system. Aerosol mists produced by ultrasonic radiation are preferred because a smaller particle size of the aerosol can be obtained with the ultrasonic radiation. For example, Anthony U.S. Patent 4,679,551 discloses an ultrasonic sprayer for producing a fine mist for moistening a mouth cavity and lips of a comatose or terminal patient. The ultrasonic sprayer is mounted in the vicinity of the oral cavity of the patient and is positioned so that a very fine particle mist settles over the oral cavity of the patient. Of course, areosol mists produced by ultrasound radiation are readily employed in non-medical applications as well.

Contact physiotherapy applies ultrasonic radiation directly to a tissue in an attempt to produce a physical change in the tissue. In conventional ultrasound physiotherapy, an ultrasonic transducer contacts the tissue via a coupling medium. Ultrasonic waves produced by the transducer travel through the coupling medium and into the tissue. The coupling medium is typically a bath of liquid, a jelly applied to the surface to be treated, or a water filled balloon. Conventional techniques provide ultrasonic waves having an intensity of about 0.25 W/cm^2 to 3 W/cm^2 at a frequency of about 1 to 3 Megahertz. The treatment is applied to a skin surface for 5 to 20 minutes, two or three times a week.

The coupling medium can provide a cooling effect which dissipates some of the heat energy produced by the ultrasonic transducer. More importantly, a coupling medium or direct contact between the tissue and the ultrasonic transducer is necessary to transmit the ultrasonic waves from the transducer to the skin surface because ambient air is a relatively poor medium for the propagation of high frequency ultrasonic waves.

Several beneficial effects have been reported from contact ultrasound physiotherapy. For example, the following effects have been

associated with contact ultrasound therapy: local improvement of the blood supply, heating of the tissue, accelerated enzyme activity, muscle relaxation, pain reduction, enhancement of natural healing processes.

Despite these beneficial effects, current techniques of medical physiotherapy using ultrasonic radiation are limited by the necessity of providing a direct contact interface between the ultrasonic transducer and the tissue to maintain an effective transmission of the ultrasonic waves from the transducer to the tissue. The necessity of direct contact (with or without) a coupling medium makes current methods cumbersome, impractical and undesirable in attempting to treat hard to reach areas and orifices. For example, it would be impractical to attempt contact ultrasound therapy on the inner surface of the ear (e.g., tympanic membrane) and middle ear to treat ear inflammation because of the inaccessibility of the surface to be treated. Moreover, the pain associated with conditions such as middle ear infections dictates avoidance of such contact therapies. Conversely, some tissue conditions may be accessible to contact ultrasound devices but would be impractical for contact ultrasound treatment. For example, open wounds resulting from trauma, burns, surgical interventions are not suitable for direct contact ultrasound treatment because of the structural nature of the open wound and the painful condition associated with those wounds. Moreover, conventional contact ultrasound may have a destructive effect on these types of open wounds due to the close proximity of an oscillating tip of an ultrasonic transducer relative to the already damaged tissue surface.

SUMMARY OF THE INVENTION

The present invention is a method of spraying a surface to deliver drugs, kill bacteria, or cleanse a surface by noncontact application of ultrasonic waves and ultrasonically activated liquids. The method applies ultrasonic radiation to a surface, such as tissue, object, or food without requiring direct or indirect (via a conventional coupling medium) contact between the ultrasonic wave transducer and the surface to be sprayed.

The method includes producing a particle spray of liquid particles produced by contact of the liquid with a free end surface of an oscillating ultrasonic transducer. The particle spray is directed onto the surface (e.g., tissue or object) while maintaining the free end surface at a distance relative to the surface to be sprayed. The ultrasonic waves cause the spray to project outwardly from the free end surface and the particles of the spray provide a medium for propagation of the ultrasonic waves emanating from the free end surface.

In the method of the present invention, directing the particle spray (created by low frequency ultrasound radiation) onto a surface kills bacteria on that surface and removes dirt and other contaminants from that surface. When the surface is a human or animal tissue, the particle spray can devlier a drug to the tissue (via the surface) in addition to killing bacteria and removing dirt and debris on the tissue surface. This method of drug delivery is particularly advantageous on tissues for which local topical application of a drug is desirable yet contact with the tissue is to be avoided. Moreover, the low frequency ultrasound radiation used in the method accentuates the action of the drug and causes penetration of the drug below the surface of the tissue. Finally, the bacteria killing method is effective when applied to a surface whether the liquid sprayed is distilled water, an antiseptic, or antibiotic.

In the method, the step of producing the spray can further include first delivering the liquid to a side surface of the transducer adjacent to the free end surface such that the liquid is pulled to the free end surface by a vacuum created by the ultrasonic waves on the free end surface of the transducer tip. The step of producing the spray can further include operating the transducer to produce longitudinal ultrasonic waves having a frequency of about 16 to 200 kilohertz with a preferred range of frequency of about 20 to 40 kilohertz. In addition, the step of directing the spray can further include maintaining a distance of separation between the free end surface of the transducer and the

surface to be sprayed of preferably about 0.5 to 10 centimeters.. The liquid can further include an antibiotic for application to the tissue. In addition, the method can include directing the spray onto the surface for about 30 to 60 seconds on a daily or semidaily basis, or at such durations, intervals, frequency, and distances as determined in the judgment of the user.

The method of the present invention permits application of ultrasonic waves to surfaces without establishing contact, directly or indirectly, between the ultrasonic transducer and the surface (e.g., tissue). For example, surfaces of the human body especially suited for treatment with the method of the present invention include infected and inflammatory processes in open wounds including firearm wounds, fire and chemical burns. In addition, the method of the present invention is particularly suited to directing a spray into orifices or other body crevices that are difficult to access. For example, inflammation of both the tympanic membrane of the ear and of the middle ear resulting from otitis media (a bacterial infection of the middle ear) are especially suitable to spray using this method. In this example, the orienting step could further include orienting the particle spray into the external auditory canal of the ear to project the spray directly onto the tympanic membrane of the ear while maintaining a distance of separation of preferably about 0.5 to 10 centimeters between the tympanic membrane and the transducer tip.

This method of spraying a surface has several advantages. First, this method topically applies medicines such as antibiotics to the tissue surface (e.g., tympanic membrane or burn wound) without the need to contact an infected and inflamed tissue with an instrument for directly applying the antibiotic to the membrane. Second, a significant bactericidal effect is observed when spraying a surface using the method of the present invention. The following bacteria, amongst others, found on the surface of human tissues have been shown to be effectively treated with the method of the present invention

including: pseudomonas aeroginesa, the family of staphylococcus bacteria, and yeast bacteria candidas albicans.

Moreover, aside from the bactericidal effect and advantages of non-contact treatment, using the method of the present invention results in a 50 to 70 percent reduction in volume used of antibiotic medicine used as compared with traditional methods for killing bacteria on a wound surface. Similarly, this allows for precise dosage of the sprayed liquid to permit a user, such as a physician to administer the desired volume of liquid at a desired rate, frequency, and duration. In addition, in cases where the liquid media consists of a mix of several different compositions, the ultrasonic radiation imparted onto the liquid media finely atomizes the different compositions to produce a uniform mixture of the different compositions that does not occur in traditional mixing methods of medicines.

The method of the present invention results in healing times for inflammatory and purulent infected wounds that is 1½ to 2 times faster than traditional methods. This effect results from a mechanical cleansing effect of the atomized spray particles which have vibratory energy due to the ultrasonic waves. The spray mechanically scrubs the surface of tissue to remove dirt, dead tissue, and purulent buildup on the tissue surface. The accentuated healing effect also results from accentuated drug delivery since the liquid medication penetrates into the tissue surface up to 1 millimeter in depth. Third, a combination of the low frequency ultrasonic waves and the insonified medicines (i.e., highly activated by ultrasonic energy) destroy the surface bacteria to result in a higher disinfecting property of insonified liquids as compared to ordinarily applied liquids. The spray of the present method also stimulates healthy cell growth to aid in granulization and epithelization of the healing tissue.

Of course, the effects of cleansing and bacteria killing are equally applicable for surfaces other than human or animal tissue. Accordingly, other

applications of the method can be directed to non-medical uses such as sterilizing surfaces of objects and food.

The significant bactericidal effect caused by the low frequency ultrasonic waves and by the highly activated state of antibiotics (produced by the ultrasonic energy) is very important. In particular, in recent years, bacteria have become increasingly resistant to traditional antibiotics applied topically (locally) or orally (systemic) due to evolution of the bacteria to overcome the antibiotics as well as over use of antibiotics in treating patients. This increases the incidence of infection and hampers control of infection in hospital and clinical settings. Accordingly, the medical community must rely on the pharmaceutical community to invent new antibiotics to treat bacteria no longer susceptible to traditional antibiotics (e.g., penicillin). Alternatively, other methods for controlling infection must be developed.

The method of the present invention offers an approach that may re-establish use of some traditional antibiotics and establish a method fighting bacteria without antibiotics when necessary. The effect of the method of the present invention in highly activating antibiotics may allow some traditional antibiotics to overcome bacteria which have become resistant to that antibiotic. Moreover, independent of the insonication effect of the antibiotics, the low frequency ultrasonic waves applied in the method of the present invention physically destroy bacteria. Bacteria are unlikely to develop a resistance to this treatment. The combination of the highly activated antibiotics and of the low frequency ultrasonic waves in the method of the present invention produce a strong bactericidal effect not found in mere topically application or orally ingested antibiotics. This combined effect has been shown to dramatically increase the healing of purulent infected wounds.

Significantly, the present method also provides a system of noncontact drug delivery without using a compression sprayer system. This simplifies the design of a noncontact drug delivery sprayer and reduces the

weight of the sprayer. More importantly, not using compression to propel the atomized particles preserves the ultrasound energy carried by the spray particles. This ultrasound energy has been proven to destroy bacteria by action of the ultrasonic waves and by highly activating the liquid medicines (e.g., antibiotics) applied to the tissue.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of an ultrasonic sprayer system for use in a method of the present invention.

FIG. 2 is a view in section of the ultrasonic sprayer as used in a method of the present invention.

FIG. 3 is an enlarged view of FIG. 2 illustrating a spray created by the sprayer of FIG. 2 in the method of the present invention.

FIG. 4 is a perspective view of the ultrasonic sprayer as used in a method of the present invention for spraying an arm.

FIG. 5 is a view of the sprayer of FIG. 3 rotated relative to a horizontal plane.

FIG. 6 is a enlarged view in section of a modification of a tip of the sprayer as used in the method of the present invention.

FIG. 7 is a enlarged view in section of a modification of a tip of the sprayer as used in the method of the present invention.

FIG. 8 is a plan view of a modified tip of the sprayer of the method of the present invention.

FIG. 9 is a plan view of a modified tip of the spray as used in the method of the present invention.

FIG. 10 is a plan view of a modified tip of the sprayer of the present invention.

FIG. 11 is a plan view of a modified tip of the sprayer of the present invention.

FIG. 12 is a plan view of a modified tip of the sprayer of the method of the present invention.

FIG. 13 is a plan view of a modified tip of the sprayer of the method of the present invention.

FIG. 14 is a plan view of a modified tip of the sprayer of the method of the present invention.

FIG. 15 is a plan view of a modified tip of the sprayer of the method of the present invention.

FIG. 16 is a plan view of a modified tip of the sprayer of the method of the present invention.

FIG. 17 is a plan view of a modified tip of the sprayer of the method of the present invention.

FIG. 18 is a plan view of a modified tip of the sprayer of the method of the present invention.

FIG. 19 is an end sectional view of a sprayer taken along line 18-18 in FIG. 2.

FIG. 20 is a sectional view of a modification of the sprayer shown in FIG. 2.

FIG. 21 is a view in section of a method of the present invention for treatment of an ear.

FIG. 22 is a photograph of a bacteria cell prior to treatment with the method of the present invention.

FIG. 23 is a photograph of a bacteria cell after treatment with the method of the present invention.

FIG. 24 is a photograph of a bacteria cell after extended treatment with the method of the present invention.

FIG. 25 is a photograph of a colony of bacteria cells after treatment with the method of the present invention.

While the above-identified figures set forth the preferred embodiments, other embodiments of the present invention are also contemplated as noted in the discussion. In all cases, this disclosure presents illustrated embodiments of the present invention by way of representation and not limitation. Numerous other modifications and embodiments can be devised by those skilled in the art which fall within the scope and spirit of the principles of this invention. The figures have not been drawn to scale as it has been necessary to enlarge certain portions for clarity. In addition, the use of such relational terms such as left/right, upper/lower, top/bottom or horizontal/vertical etc. are used herein for reference purposes only and are not intended to be limiting features of the invention disclosed.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

1. Spraying a Surface to Kill Bacteria, Deliver a Drug, and Cleanse the Surface.

A spraying system used in a method of the present invention is illustrated in FIG. 1 generally at 10. The spraying system 10 is used for spraying liquids onto a surface and delivering ultrasonic radiation to a surface. The system 10 includes an ultrasonic generator 12, a power cord 14, and a hand held sprayer 16. The ultrasonic generator 12 includes a power switch 18, controls 20, and a display 22. The power cord 14 includes a first end 24 and a second end 26. The sprayer 16 has a first end 28, a second end 30, a housing 31, and a liquid delivery mechanism 32. The liquid delivery system 32 includes an arm 34, a mounting 36 (including a spring), and reservoir 38. The reservoir 38 includes a pin 39. The arm 34 of the system 32 includes a first end 40, a second end 42, and bent portion 44 between the ends. The sprayer 16 is a modification of a device for ultrasonic atomization of a liquid medium as disclosed in U.S. Patent 5,076,266. The subject matter of U.S. Patent 5,076,266 is herein incorporated by reference in the present application.

The first end 24 of the power cord 14 is electrically connected to the ultrasonic generator 12 and the second end 26 of the power cord is electrically connected to the first end 28 of the sprayer 16. The bent portion 44 of the arm 34 of the liquid delivery system 32 is rotatably mounted to the housing 31 of the sprayer 16 via mounting 36. The second end 42 of the arm 34 is connected to the pin 39 on top of the reservoir 38. The reservoir 38 is fixed to the second end 30 of the sprayer 16.

The ultrasonic generator 12 includes electrical circuitry known in the art for producing an electrical signal to cause longitudinal ultrasonic sound waves in the frequency of 16 to 1000 kilohertz on an ultrasonic transducer. The controls 20 permit selection of the frequency as desired. The display 22 shows the current frequency of the signal produced by the generator 12. The power cord 14 provides an electrical connection between the generator 12 and the sprayer 16 for carrying the signal produced by the generator 12. The sprayer 16 includes means for receiving the signal from the generator 12 and producing ultrasonic waves to create an atomized particle spray of liquid.

To produce a spray, the second end 40 of the arm 34 of delivery system 32 is pressed downward causing rotation of the arm 34 about the mounting 36 and a lifting of the arm end 42 and the pin 39 atop the reservoir 38. This causes liquid to flow out of the reservoir 38 and come into contact with the ultrasonic transducer inside the sprayer 16 to produce a spray from the second end 30 of the sprayer 16. The spray stops upon releasing the arm 34 due to the bias of the spring in mounting 36 which returns the liquid delivery system to a closed state.

FIG. 2 further illustrates the sprayer 16. The liquid delivery system 32 of the sprayer 16 includes the arm 34 and the reservoir 38. The reservoir 38 has a lower portion 46, an upper portion 48, and a top plate 50 including an aperture 51. A liquid 52 is held within the reservoir. The pin 39

has a lower end 54, an upper end 56, and a collar 57. The end 42 of the arm 34 also includes an aperture 58.

The second end 30 of the sprayer 16 further includes an upper portion 60 and a channel 62 with an opening 63. A shroud 61 extends from the upper portion 60. The second end 30 of sprayer 16 also includes an aperture 64, an inner wall 65, a bellmouth 66, and a cavity 68 within the housing 31. The sprayer 16 also has an ultrasonic transducer 70 including a concentrator 71 and a vibrator 73. The concentrator 71 includes a tip 74 having a free end surface 75 and a side surface 76.

The top plate 50 is secured within the upper portion 48 of the reservoir 38. The upper end 56 of the pin 39 extends through and is slidably received within the aperture 51 of the top plate 50 and the aperture 58 of the end 42 of the arm 34. The collar 57 of the pin 39 secures the pin 39 onto the end 42 of the arm 34. The pin 39 extends through the reservoir 38 and the lower end 54 of the pin 39 removably fits within the opening 63 of the channel 62. The channel 62 is in fluid communication with the aperture 64 at the second end 30 of housing 31. As shown, the lower end 54 of the pin 39 blocks the opening 63 of the channel 62.

The transducer 70 extends through the cavity 68 of the housing 31 with the tip 74 of the concentrator 71 extending coaxially through the aperture 64. The free end surface 75 of the concentrator 71 is disposed at an open end of the aperture 64. The side surface 76 of the tip 74 is disposed adjacent the channel 62. The bellmouth 66 is secured within the cavity 68 of the housing 31 to the inner wall 65 of the housing 31 and encompasses the concentrator 71.

The ultrasonic transducer 70 selectively produces longitudinal sound waves in the ultrasonic frequency range. The sound waves are produced by the ultrasonic vibrator 73 (initiated and controlled by a signal from the ultrasonic generator 12) and are focused as the waves travel through the

concentrator 71 toward the tip 74 of the transducer 70. The waves travel through the transducer 70 to the free end surface 75 of the transducer 70 where the waves meet the interface of the transducer 70 and the surrounding ambient environment. The bellmouth 66 further focuses the waves emanating from the free end surface 75 of the transducer 70.

FIG. 2 illustrates the liquid delivery system 32 in a first closed position in which the end 54 of the pin 39 blocks the opening 63 of the channel 62 thereby preventing flow of the liquid 52 into the channel 62. Accordingly, although the ultrasonic transducer 70 may be producing ultrasonic waves at the free end surface 75, no spray of liquid is produced in this first closed position of the liquid delivery system 32.

FIG. 3 illustrates the liquid delivery system 32 of the sprayer 16 in a second open position in which the end 54 of the pin 39 permits the liquid 52 to flow into the channel 62 to produce a spray 80 of particles 82 upon contact of the liquid 52 with the transducer 70. In particular, as shown in FIG. 3, when the first end 40 of the arm 34 is pressed downwardly relative to the housing 31, the biasing action of the spring mounting 36 is overcome and the second end 42 of the arm is rotated clockwise via the rotatable mounting 36. This results in the top plate 50 and the pin 39 being directed upwardly, moving the pin 39 into a second position in which the liquid 52 can flow down the channel 62, in the form of droplets 83 of the liquid 52, into the aperture 64 of the second end 30 of the housing 31. The droplets 83 of liquid 52 contact the side surface 76 of the transducer tip 74 adjacent the free end surface 75. The fluid 52 is not under pressure or compression within this sprayer system 10. In particular, the fluid reservoir 38 is not pressurized such that the liquid passing through channel 62 to side surface 76 of transducer tip 74 does so by simple gravitational forces.

The ultrasonic transducer 70 of the sprayer 16 produces longitudinal ultrasonic waves that emanate from the free end surface 75 of the

transducer tip 74. As seen in FIG. 3, the free end surface 75 is directly exposed to the surrounding environment, i.e., is not enclosed within the second end 30 of housing 31. The ultrasonic waves can have a frequency in the range of 16 kilohertz to 200 kilohertz but are preferably in the range of 16 to 150 kilohertz. A most preferred range is from 16 to 40 kilohertz and the most preferred frequency is about 26 kilohertz. The amplitude of the waves is preferably about fifty microns produced with an intensity of about 1.5 W/cm^2.

Upon contact with the side surface 76 of transducer tip 74, the droplets 83 become more finely dispersed to form smaller droplets 84. The droplets 84 of liquid (e.g., antibiotic or other liquid) become "insonified", i.e., become highly activated, when in contact with the oscillating transducer tip 74 because of the vibratory energy on the transducer tip 74. The ultrasonic waves emanating from the free end surface 75 of transducer tip 74 create a negative pressure (i.e., vacuum force) on the free end surface 75. This vacuum effect pulls the insonified droplets 84 of liquid 52 from the side surface 76 onto the free end surface 75. Once on the free end surface 75, the longitudinal waves emanating from the oscillating free end surface 75 cause the droplets 84 of the liquid 52 to become even more finely dispersed, i.e., atomized, and to be forcefully jettisoned or directed outwardly into the ambient environment away from the free end surface 75 in the form of the spray 80 of particles 82. After this initial forceful jettisoning, the atomized particles 82 of the liquid 52 are further pushed through the air by the longitudinal ultrasonic waves emanating from the transducer tip 74 at free end surface 75. As seen in FIG. 3, the particle spray 80 projects outwardly from the transducer tip 74 in a direction substantially parallel to a longitudinal axis of the sprayer 16. The atomized spray 80 in combination with the ambient air provides a medium for allowing propagation of (i.e., transmitting) ultrasonic waves emanating from the free end surface 75. To stop the flow of liquid into the channel 62 and thereby stop the production of the spray 80, the arm portion 40 is released thereby causing the

pin 39 to move downwardly into the first closed position to block opening 63 and close access to the channel 62.

As seen in FIG. 3, the spray 80 projects horizontally from the transducer tip 74 of the sprayer 16 and carries the ultrasonic waves emanating from the free end surface 75. The spray 80 projects outwardly from the transducer tip 74 onto a surface 85 of a tissue 86. The sprayer 16 is held relative to the tissue 86 so that a distance of separation D1 is maintained between the surface 85 of the tissue 86 and the free end surface 75 of the transducer tip 74. The distance of separation between the tissue surface 85 and the free end surface 75 of the ultrasonic transducer is preferably about 0.5 to 10 centimeters but can extend up to 15 to 20 centimeters as deemed necessary by the user. At a minimum, the distance of separation should be at least 1 millimeter so that contact is avoided. Under these conditions, the liquid spray 80 projects toward the tissue surface 85 and a combination of the liquid spray and the ambient air carry, i.e., facilitate propagation of, the ultrasonic waves from the free end surface 75 of the transducer tip 74 from the sprayer 16 onto and into the tissue surface 85. The projected spray 80 of the liquid antibiotic 52 causes the liquid 52 to penetrate the tissue surface 85 at a depth D3 of about 1 millimeter and causes the ultrasonic waves to similarly penetrate the skin at a depth D3 of about 1 millimeter. (See FIG. 3).

The volume of the spray 80 can be increased or decreased by controlling the rate at which the liquid 52 is directed to the free end surface 75. A respective depressing or uplifting of the arm second portion 40 causes a respective opening and closing of the channel 62 by the pin 39. When the pin 39 is raised from its first closed position, fluid 52 flows through the channel 62 and onto the side surface 76 of transducer tip 74 and is ultimately atomized off free end surface 75. Selective lowering of the pin 39 within the reservoir 38 reduces the amount of liquid 52 flowing into the channel 62 and reaching free end surface 75 thereby reducing the volume of spray 80.

A method of the present invention of spraying a surface can be illustrated with a method of spraying an open wound of a human arm as illustrated in FIGS. 3 and 4. As shown in FIG. 4, the sprayer 10 is brought into proximity with an arm 87A having an open wound 87B. The open wound 87B can be a burn wound or other skin surface condition in which normal healing of the skin surface fails to occur and in which killing bacteria on the wound, delivering antibiotics to the wound, and cleansing the wound is critical. In this example, the open wound is a purulent infected wound resulting from trauma in which the surface of the skin has been scraped off the arm thereby creating the open wound surface 87B. The wound surface can have several bacteria and pathogenic flora acting on the exposed tissue preventing the normal healing processes and causing purulent inflammation of the wound 87B. The most common bacteria include staphylococci (strains aureus and epidermis) and pseudomonas aeruginosa as well as pathogenic microflora including gram-positive diplococci, gram-negative bacilli.

The first step of the method includes providing a liquid for spraying the open wound 87B. The liquid 52 typically includes a single medicine or a combination of medicines such as antibiotics, oxidants, antimicrobials, as well as sulfanilamides. The liquid 52 is placed in the reservoir 38 of the sprayer 16. The liquid 52 can also include distilled water alone or in combination with antibiotics or another medicinal agent.

The next step of the method for spraying the open wound includes directing the liquid, e.g., antibiotics, to the free end surface of the transducer tip wherein an atomized particle spray of the liquid is created upon contact of the liquid with the free end surface of the transducer. Particles of the spray carry the ultrasonic radiation imparted by the free end surface. As shown in FIG. 3, directing the liquid 52 to the free end surface 75 includes the following steps. Upon depressing arm portion 40, the pin 39 is moved from its first closed position (FIG. 2) to the second open position (FIG. 3) allowing droplets

83 of the liquid antibiotic 52 to travel down the channel 62 and onto the side surface 76 of the concentrator 71 at the transducer tip 74. The particles 82 are insonified, i.e., highly activated, upon contact with the side surface 76. Next, as described in association with FIG. 3, the method further includes the liquid droplets 84 being pulled to the free end surface 75 by a vacuum effect (i.e., negative pressure) resulting from ultrasonic waves emanating from the free end surface 75. Upon contact of the liquid droplets 84 with the free end surface 75, the spray 80 of particles 82 is produced and projects outwardly from the free end surface 75 as seen in FIG. 3.

The method of the present invention for spraying the open wound 87B further includes the step of orienting the particle spray directly onto the tissue 87B while maintaining a distance of separation between the tissue 87B and the free end surface 75 of the transducer 70. As seen in FIG. 4, the spray 80 projects horizontally from the second end 30 of the sprayer 16. Orienting the spray 80 includes holding the sprayer 16 manually (or with an instrument) so that the spray 80 projecting outwardly from the transducer tip 74 of the sprayer 16 is aimed at the surface of wound 87B on arm 87A. The sprayer 16 is held relative to the wound 87B so that a distance of separation is maintained between the wound 87B and the free end surface 75 of the transducer tip 74 of the sprayer 16. The method further includes holding the sprayer 16 so that the distance of separation between the wound 87B and the free end surface 75 of the ultrasonic transducer is preferably about 0.5 to 10 centimeters. The distance can extend up to 15-20 centimeters if necessary although these larger distances (15-20) are not preferred. In any case, the user of the device can use their judgment and skill and select the appropriate distance. At a minimum, the distance of separation should be at least 1 millimeter to avoid contact. Under these conditions, the liquid spray 80 projects toward the wound surface 87B and a combination of the liquid spray and the ambient air carry, i.e., facilitate propagation of, the ultrasonic waves from the free end surface 75 of the

transducer tip 74 from the sprayer 16 onto and into the wound surface 87B. The projected spray 80 of the liquid antibiotic 52 causes the liquid 52 to penetrate the wound surface 87B at a depth of about 1 millimeter and causes the ultrasonic waves to similarly penetrate the skin at a depth of about 1 millimeter. FIG. 3 schematically illustrates this penetration.

The step of orienting the spray includes orienting the spray onto the wound 87B for about 30 to 60 seconds and up to five minutes. Although the spray 80 can be oriented onto the wound 87B for less than 30 seconds (e.g., 5 or 10 seconds) or more than 5 minutes, the range of 30 seconds to five minutes is preferred. As needed, the user can select the duration of treatment and distance of separation as well as the volume administered. The spray can be oriented onto the tissue either by maintaining the sprayer 16 in a position stationary relative to the wound 87B or by using a back and forth sweeping motion of the sprayer 16 to cover a larger entire wound surface 87B.

Moreover, the step of orienting the spray can further include orienting the spray upwardly (toward the vertical) at an inclined angle directly onto a tissue. As schematically depicted in FIG. 5, the sprayer 16 can be manually held such that the longitudinal axis of the housing 31 is at an angle (e.g., 30°) relative to a horizontal plane A-A to cause the spray 80 to be forcefully directed onto the tissue surface 85 (e.g., wound 87B). This allows flexibility in orienting the spray 80 onto the tissue 85. Similarly, although not shown, the sprayer 16 can be oriented downwardly at an angle directly onto the tissue 85. Although the sprayer 16 used in the method of the present invention is a compressionless system (no liquid pressure or air pressure), the operability of the sprayer 16 can be maintained despite the incline angle of the sprayer 16 because of the phenomenon at the free end surface 75. In particular, the vacuum (negative pressure) created by the low frequency ultrasonic waves at the free end surface 75 of transducer tip 74 are sufficiently strong to pull the droplets 84 of liquid on the side surface 76 to the free end surface 75. This

vacuum force overcomes gravitational forces which would ordinarily be expected to pull the droplets 84 on the side surface 76 away from the free end surface 75. Accordingly, the method of the present invention includes orienting the spray upwardly or downwardly onto a tissue while still maintaining forceful projection of the spray without compression of liquid delivered to the free end surface and without air pressure conventionally used to direct a spray.

The free end surface 75 of the transducer tip 74 preferably is cylindrical in shape and has a diameter of about 1 centimeter. With ultrasonic waves having a frequency of about 16 to 200 kilohertz, an intensity of radiation of about 1.5 W/cm^2 is provided over the free end surface 75 to produce ultrasonic waves having an amplitude of about 50 microns. This produces a particle size of the spray of about 5 microns and a spray cone length of about 40 centimeters.

A significant bactericidal effect occurs by application of liquids on infected and inflamed tissue, as well as non-biological surfaces, using the method of the present invention. The method produces two bacteria killing effects. First, the low frequency ultrasonic waves carried to the tissue physically destroy bacteria on the tissue surface 84 and up to 1 millimeter below the tissue surface 85. The ultrasonic waves are believed to cause cavitational and/or microstreaming effects in the bacteria which disrupt the bacteria cells. This effect is maximized when the frequency is from 16 to 40 kilohertz and particularly at 26 kilohertz. However, at least some effect is achieved in the frequency range of 40 kilohertz to 200. For example, in the frequency range of 40 to 100 kilohertz, the bactericidal and healing effect is about 80 percent of the maximum effect obtained in the range from 16 to 40 kilohertz. Similarly, a frequency range of 100 to 150 kilohertz used with the method of the present invention achieves an effect about 50 percent of the maximum effect achieved in the frequency range of 16 to 40 kilohertz. Although a frequency of 16 up to

20 kilohertz can be used, this range is generally avoided because the sound waves may be uncomfortable to the patient and operator.

Second, the bactericidal effect results, in part, from the "insonication" of antibiotics in the method of the present invention. Antibiotics "insonified" in the method of the present invention become highly activated and have an increased effectiveness over conventionally applied antibiotics. Accordingly, although the atomized particle spray can be created by delivering the liquid 52 directly to the free end surface 75, it is particularly advantageous to first deliver the liquid 52 to the side surface 76 a predetermined distance (e.g., D2 in FIG. 3) from the free end surface 75 of the transducer tip 74. By delivering the liquid 52 first to the side surface 76, the liquid droplets 83 of antibiotic become "insonified", i.e., highly activated, from vibratory ultrasonic radiation on the side surface 76 of transducer tip 74. Accordingly, because the liquid droplets 84 maintain contact with the transducer tip 74 as they move to the free end surface 75, the droplets 84 of antibiotic remain "insonified", i.e., highly activated. This activated state is retained as the droplets become particles and are projected from the free end surface 75. However, when the liquid 52 is delivered directly to the free end surface 75 without first being delivered to the side surface 76, the liquid particles lack the "insonification" phenomena of the liquid particles created when the liquid 52 is first delivered to the side surface 76. Insonified antibiotics are highly activated and increase the effectiveness of antibiotics as compared with traditionally applied antibiotics (oral ingestion or direct topical). Accordingly, the method comprises a highly desirable form of drug delivery.

The significant bactericidal effect caused by the low frequency ultrasonic waves and by the highly activated state of antibiotics (produced by the ultrasonic energy) is very important. In particular, in recent years, bacteria have become increasingly resistant to traditional antibiotics applied topically (locally) or orally (systemic) due to evolution of the bacteria to overcome the

antibiotics as well as over use of antibiotics in treating patients. This increases the incidence of infection and hampers control of infection in hospital and clinical settings. Accordingly, the medical community must rely on the pharmaceutical community to invent new antibiotics to treat bacteria no longer susceptible to traditional antibiotics (e.g., penicillin). Alternatively, other methods for controlling infection by killing bacteria must be developed.

The method of the present invention offers an approach that may re-establish use of some traditional antibiotics and establish a method fighting bacteria without antibiotics when necessary. The effect of the method of the present invention in highly activating antibiotics may allow some traditional antibiotics to overcome bacteria which have become resistant to that antibiotic. Moreover, independent of the insonication effect of the antibiotics, the low frequency ultrasonic waves applied in the method of the present invention physically destroy bacteria. Bacteria are unlikely to develop a resistance to this treatment. The combination of the highly activated antibiotics and of the low frequency ultrasonic waves in the method of the present invention produce a strong bactericidal effect not found in mere topically applied or orally ingested antibiotics. This combined effect has been shown to dramatically increase the healing of purulent infected wounds.

The method of the present invention can also be used in conjunction with systemic antibiotic therapy to provide a more aggressive treatment course. Alternatively, the method can be applied instead of systemic antibiotic therapy in cases where such systemic treatment is ineffective (e.g., superinfections) or where the side effects of systemic antibiotics (nausea, diarrhea, gastro intestinal upset) are to be avoided. Although the bactericidal effect resulting from the method of the present invention is more effective when the liquids applied include antimicrobials, oxidants, and antibiotics, as well as antiseptics, this bactericidal effect also occurs when the liquid used is distilled water because of the physical effect of the low frequency ultrasonic waves.

This is particularly advantageous for patients that have serious allergies to traditional antibiotics or patients that have superinfections from bacteria resistant to the available antibiotics.

When used in a complete course of treatment of a wound by a physician or other user, the method of the present invention results in several effects upon the purulent infected tissue surface of the wound. First, the method results in a quick separation of dead tissue (tissue detritus) and clears away pus and destructured tissue elements. The method also causes cupation of the suppurative and inflammatory center. As observed in morphological and immuno-cetochemical studies, the method results in a sharp intensification of cell immunity reaction and stimulates active proliferation of connective tissue, which revascularizes and replaces the wound tissue. Observed effects include an increased quantity of macrophagial and microphagial cells and fiber layers in the connective tissue as well as an increase in collagenous fiber content, elasticity content, and density of the hemocapillary distribution. The method also accelerates granulation and final epithelization in the wound tissue zone. The combination of these effects results in wound healing about one and one-half to two times as fast as healing resulting from traditional wound treatment (topical dressings and systemic antibiotics).

The accelerated healing effect results from a combination of at least three phenomena. First, the method produces a mechanical scrubbing action on the wound surface because of the low frequency ultrasonic wave energy reaching the wound surface and because the spray particles are forcefully directed into the wound surface by the ultrasonic waves. This mechanical scrubbing action is responsible for the quick separation of the dead tissue, dirt, and destructured elements from the wound. Moreover, this mechanical effect stimulates healthy tissue growth by accelerating the normal healing process of the wound. Second, a combination of the low frequency ultrasonic waves and the insonified medicines (i.e., highly activated by ultrasonic energy) destroys the

surface bacteria to result in a higher disinfecting property of the insonified medicines as compared to ordinarily applied liquids. Third, the method of the present invention also causes the liquid medication as well as the ultrasonic waves to penetrate the tissue up to 1 millimeter in depth.

Two of these effects are advantageous in spraying surfaces other than human tissue. The cleansing effect can be used to clean surfaces of objects by removing dirt and the bacteria-killing effect can be used to disinfect surfaces by killing bacteria on the surface.

Moreover, when the surface to be sprayed is human tissue, a prophylactic effect of the method actively prevents the development of purulent and inflammatory complications of wounds on human tissue. This effect is achieved because the method of the present invention effectively suppresses the virulency and ability to multiply of pathogenic flora (e.g., streptococcus bacteria) on the surface wound. In particular, in cases of managing tissue wounds resulting from surgery, treatment of the wound surface with the method of the present invention immediately after wound creation completely prevented suppurative and inflammatory infectious complications.

This prophylactic effect is particularly significant for surgery in a nonsterile atmosphere such as field use or in less developed countries not having highly sterile operating rooms. In those situations, virtually every surface (human or otherwise) is laden with bacteria. Killing bacteria on the patient and other surfaces is very important.

This prophylactic effect of the insonified medicines is particularly effective where the surface wound 87B is a burn wound (thermal, chemical, or electrical). The method provides a prophylactic effect of complications for burns of the first, second, third, and fourth degrees. The wounds can be treated twice a day using the method of the present invention just prior to application of sterile bandages. The sprayed liquid can include a combination of oxidizers, antibiotics, and antimicrobial agents. This prophylactic effect in burn wounds

is significant because infection is a major cause of serious illness and death resulting from burn wounds. The problem results from the inability of the open wound to ward off growth of bacteria and the inability of new skin to form to cover the wound surface to limit bacteria growth.

This prophylactic effect on suppurative and inflammatory processes is critical in surgical wounds, open fractures, wounds including stab wounds, and burns of all degrees and types (thermal, chemical, and electrical). Although the present example illustrates the method of the present invention in treating an open wound (e.g., burn, trauma, surgery) on a limb such as arm, the method can be applied to any open wound or surface tissue condition accessible to the method of the present invention.

Moreover, aside from the bactericidal effect and advantages of non-contact treatment, using the method of the present invention results in a 50 to 70 percent reduction in volume used of antibiotic medicine used as compared with traditional dressing methods. Similarly, the method also allows for precise dosage of the sprayed liquid. A user can deliver the desired volume of liquid at a desired rate and duration. In addition, there is complete flexibility in the frequency of application as well as the choice of drug (or even no drug). In addition, in cases where the liquid media consists of a mix of several different compositions, the ultrasonic radiation imparted onto the liquid media finely atomizes the different compositions to produce a uniform mixture of the different compositions that does not occur in traditional mixing methods of medicines.

The method of the present invention provides a method of compressionless non-contact drug delivery. In particular, in the method of the present invention, the liquid 52 is not under compression during delivery from the fluid reservoir 38 to the transducer tip 74. In addition, the spray 80 is neither created nor directed with a compressed air system found in conventional spray nozzles. Rather, the spray 80 is created solely by the stress produced on

the free end surface 75 by the longitudinal ultrasonic waves emanating therefrom. This lack of compression or pressure is important in preserving the energy of ultrasound waves propagating through the atomized spray as well as preserving the highly activated state of the insonified liquids caused by the oscillating transducer tip 74 of the sprayer 16 used in the method of the present invention. This compressionless, non-contact method of the present invention has been proven to destroy bacteria by action of the ultrasonic waves and by highly activating the liquid medicines (e.g., antibiotics) applied to the tissue.

In addition, the compressionless feature of the method of the present invention has other important advantages. For example, traditional application of liquid medicines (e.g., antibiotics) by spraying methods (e.g., aerosol can, compression sprayer) produce a ricochet effect of the medicine in which the spray particles from the spray source bounce off the tissue because of the pressure directing the spray. The rebounding spray particles can travel onto an exposed skin surface (e.g., arm, eye) of the technician (applying the spray) or become airborne to be inhaled by the technician. Over time, the technician can receive a harmful dose of the medicine through this ricochet effect of traditional aerosol sprayers. In contrast, the compressionless spray 80 produced in the method of the present invention does not cause the spray particles 82 to ricochet off the tissue to be treated. Rather, in the method of the present invention, the spray particles 82 have sufficient energy to penetrate the tissue yet do not have energy sufficient to rebound off the tissue.

Moreover, the method of the present invention provides a way to produce an aerosol form of medicines for delivery to tissue without using chloroflourocarbons, which are responsible for deterioration of the ozone layer.

The sprayer used in the method of the present invention can include modifications of the diameter of the free end surface 75 of the transducer tip 74. In particular, the diameter of the transducer tip can range from 1 millimeter to 40 millimeters. For example, to produce a length of a

spray cone of about 40 centimeters, a tip of about 1 centimeter diameter is preferred. In this example, the power applied to the transducer 22 is regulated so that an intensity of radiation is delivered to the free end surface 75 of the transducer tip 74 at about 1.5 W/cm^2 and the amplitude of ultrasonic waves is preferably about 50 microns.

The spray cone length can be adjusted as desired (by regulating the amplitude of ultrasonic waves) to correspond with the optimum distance of separation between the transducer tip and the surface to be treated. One factor in changing the spray cone length is the diameter of the tip 74. Accordingly, a different tip size may be used when attempting to achieve a different spray cone length. In general, smaller diameter tips are preferred when generating a longer spray cone. However, the primary factor in determining spray cone length is the amplitude of the ultrasonic waves, which can be controlled by the ultrasonic generator. In addition, the spray cone length can be affected by the size of atomized particles wherein a larger particle size (e.g., 10 microns) will result in a longer spray cone than a smaller particle size (e.g., 3-5 microns) because the larger particles tend to travel farther. A larger particle size is achieved by increasing the delivery rate of the liquid to the transducer tip. Accordingly, although the diameter of the tip can be varied as desired, it is but one factor in controlling the spray cone length of the spray.

The method of the present invention which uses sprayer 16 also can include several modifications. The configuration of the distal end of the sprayer 16 can be modified to affect differences in the spray cone generated by the free end surface 75. In particular, by securing the bellmouth 66 about the transducer tip 74 on an interior surface 65 of the second end 30 (as shown in FIGS. 2 and 3) creates a narrower spray cone of the atomized particle spray than would occur without the bellmouth 66 (see also FIG. 6). This permits a user to more precisely direct the particle spray as desired because of the more focused spray cone. In addition, this configuration increases the length of the

spray cone of the atomized particle spray thereby permitting an increased distance of separation between the transducer tip 74 and tissue to be treated while still maintaining the propagation of ultrasonic waves and delivery of atomized particles.

Alternatively, as seen in FIG. 7, a bellmouth 88 can be fixed on an exterior surface 90 of the second end 30 of the housing 31. In this case, the bellmouth 88 encompasses the transducer tip 74 and has an open portion 92 facing outwardly into the ambient environment. The free end surface 75 is disposed concentrically within the bellmouth 88. This configuration shown in FIG. 7 results in a spray cone which is relatively wider and shorter than the spray cone resulting from the configuration shown in FIGS. 2 and 3.

In addition, the free end surface 75 of transducer tip 74 can be modified from a flat surface (FIGS. 2 and 3) to a preferred truncated cone shape as shown in FIG. 8. The free end surface 94 has an inclined side surface 96 extending between the side surface 76 and the free end surface 94. This surface 96 facilitates distribution of the liquid media circumferentially about the periphery of the free end surface 94. The surface 96 allows a greater volume of fluid to be atomized uniformly because of the increased peripheral distribution of the liquid media from side surface 76 of the transducer tip 74 as it descends along surface 96. Accordingly, with this preferred configuration, the liquid media more uniformly approaches the free end surface 94 around the entire edge of the surface 94 as compared to a flat end surface such as free end surface 75 shown in FIGS. 2 and 3.

The most preferred configuration includes the truncated cone shape free end surface 94 of the transducer tip in combination with either the bellmouth 66 (FIG. 6) or the bellmouth 88 (FIG. 7) encompassing the transducer tip. These preferred configurations maximize distribution of a liquid onto its free end surface while also minimizing or maximizing a spray cone angle and length as desired.

In addition, to achieve slightly different spray patterns and particle size distributions, the free end surface 75 can be modified into other surface shapes. As shown in FIGS. 9-18, a variety of transducer tips 74 are shown each having a different shaped free end surface. FIG. 9 illustrates a transducer tip 74 having a free end surface 98 in the shape of a concave inclined surface. This surface 98 is most suited for when the liquid 52 is delivered to the free end surface 98 in the form of a stream instead of droplets. The incline of the surface makes it easier to receive the delivery stream and the concave shape provides an increased surface area for improving the "insonification" of the liquid 52 because the liquid 52 remains in contact with the transducer 70 for a longer period of time as compared to a flat surface. FIG. 10 illustrates a transducer tip 74 having a free end surface 100 which is inclined relative to the longitudinal axis of the transducer tip 74 yet is relatively flat (as compared to concave free end surface 98 of FIG. 8). This surface 100 facilitates delivery of the liquid in stream form because the surface is tilted toward the source of the stream. FIG. 11 illustrates a transducer tip 74 having a free end surface 102 in the shape of a cone. In general, the cone shaped surface 102 provides a wider angle spray cone, although the width of the spray cone depends on the angle of the cone. FIG. 12 shows a transducer tip 74 having a free end surface 104 in the shape of an ellipsoid of revolution, i.e., a concave curved surface in the shape of a bowl. This concave shape focuses to ultrasonic waves to a focal point beyond the free end surface 104 to accentuate penetration of the ultrasonic waves below a tissue surface.

FIG. 13 illustrates a transducer tip 74 having a free end surface 106 in the shape of a convex hemispherical surface. This surface results in a spray that is more uniform and distributed in a hemispherical shape rather than a cone shape (shown in FIG. 3). FIG. 14 illustrates the transducer tip 74 in its modified form having a free end surface 108 in the shape of a cone having concentrically arranged ring surfaces 110. This surface results in a spray in the

form of a spiral for producing a higher pressure spray. FIG. 15 shows a transducer tip 74 having a free end surface 112 having an inclined surface relative to the longitudinal axis of the transducer tip 74 wherein the surface includes a concave curvature and includes ridges 114 on the free end surface 112. FIG. 16 shows a transducer tip 74 having a free end surface 116 that is inclined relative to the longitudinal axis of the transducer tip 74 and further includes a plurality of steps 118 formed in the inclined surface 116. The surfaces 112 (with ridges 114) and 116 (with steps 118) increase the contact time of the liquid with the free end surface to accentuate the insonication of the liquid particles. FIG. 17 shows a transducer tip 74 having a free end surface 120 having a undulating surface shape. This surface produces a mixing of ultrasonic wave characteristics of diffraction, interference, etc. FIG. 18 shows a transducer tip 74 having a free end surface 122 having stepped indentations 124. This surface produces a pulsed-type spray because particles leaving the troughs of the steps 124 have different energy levels than the particles leaving the tops of the steps 124.

In addition, one of the bellmouth arrangements (66 of FIG. 6 or 88 of FIG. 7) can encompass the transducer tip 74 of one of modified free end surface embodiments in FIGS. 9-18 to further alter the spray cone as desired.

The method of the present invention can further include simultaneously or selectively directing multiple liquids to the free end surface of the ultrasonic transducer. As shown in FIG. 19 (an end sectional view), the sprayer 16 of FIG. 2 has been modified so that channels 62B and 62C are provided, in addition to channel 62A, for delivering a liquid to the side surface 76 and/or free end surface 75. Accordingly, channel 62B directs liquid B to the transducer tip 74 and channel 62C directs liquid C to the transducer tip 74. This arrangement is especially suited for simultaneously delivering liquids (e.g., A, B, C) to the transducer tip 74 where each liquid has a different viscosity so that a uniform mixture of the liquids can be produced at the transducer tip.

Alternatively, this arrangement can permit several liquids to be selectively directed to the transducer tip 74 for applying several liquids, one at a time, in series to a tissue surface. In addition, the liquid 46 need not be delivered to the top side of the transducer tip 74 (see FIGS. 2 and 3) but rather can be delivered from any direction (e.g., top, side, bottom, etc.) relative to the transducer tip 74 (FIG. 19).

FIG. 20 illustrates a modification of the sprayer 16 of FIG. 2 to include delivery of the liquid 52 to the bottom of the transducer tip 74. As seen in FIG. 20, the modified sprayer housing 31 includes a tube 125, a channel 126, and a pressure bulb 127. The channel 126 extends from the aperture 64 to an opening 128 in the housing 31. One end of the tube 125 is connected to the housing 31 at the opening 128 and a second end 129 of the tube 125 is connected to the bulb 127. The bulb 127 includes a cavity for holding the liquid 52. To deliver the liquid 52, the bulb 127 is squeezed to force the liquid out of the bulb 127 into the tube 125 and through the channel 126. The tube 125 and bulb 127 are configured to deliver the liquid 52 such that liquid 52 arrives at the side surface 76 of the transducer tip 74 with little or no pressure. The liquid is then delivered to the free end surface 75 by the vacuum effect of the ultrasonic waves as previously described in association with FIGS. 2 and 3. This modified configuration of liquid delivery can provide an alternative delivery system to the delivery system 32 as orientation (e.g., vertical, angled) of the sprayer 16 warrants.

Virtually any medicines or liquids can be applied using the method of the present invention. As always, the type of medicine used depends on the pathology of the disease, its location, and the stage of the suppurative and inflammatory processes on the wound. Typically, an antibiotic, antimicrobial, oxidant, and sulfanilamides are applied separately or in combination.

Antibiotics, among others, suitable for use in the method of the present invention include ampicillin, sodium salt, microcide, ceporin (u), tetracycline hydrochloride, neomycin sulfate, kanamycin, gentamycin, erythromycin, levomycetin, polymican, M sulfate, gramicidin.

Antiseptics, among others, suitable for use in the method of the present invention include iodinal, hydrogen peroxide, hydroperie, salicylic acid solution, sodium tethraborate, methylene blue, green brilliantine, ethacridine lactate, chlorhexadine, novoimanine, baliz-2, sanguirythrin, lisozyme, tincture of Japanese sophora.

Sulfanilamides, among others, suitable for use in the method of the present invention include soluble streptocide, sodium norsulfazole, sulfazine, sodium sulfate, furaplast, furacillin.

Finally, anti viral medicines include oxolin for treating viral rhinitis.

In addition to the method of the present invention of spraying a surface as discussed thus far, the method of the present invention can be used for spraying other biological surfaces such as an ear, nasal and sinus cavities, oral cavity, vagina, and an eye. In each of these other methods, some steps of the method are substantially the same as those described for the method already discussed. In particular, the steps of providing a liquid, providing a source of low frequency ultrasonic waves, and delivering the liquid to the free end surface of the ultrasonic transducer to create a spray are generally common to all of the methods of the present invention for spraying a surface to kill bacteria and/or deliver a drug.

2. Killing Bacteria and Delivering a Drug Within an Ear

In one application of the method of the present invention, the surface to be sprayed includes the middle ear and external ear. In particular, the method is useful in spraying the tympanic membrane (i.e., ear drum), and the external auditory canal. This condition is very painful, and if not treated,

can result in dizziness and partial hearing loss. The condition also results in a suppurative, i.e., pus-like discharge which can create an offensive odor. The condition typically results from infection and fluid build up in the middle ear when the eustachian tube becomes blocked, preventing fluid drainage from the middle ear. Traditional methods of treatment of the symptoms include mechanical abrasive cleansing of suppuration on the external auditory canal. However, infections of the middle ear are interior of the tympanic membrane, and therefore require treatment either by systemic antibiotics (i.e., orally ingested) or by making an incision in the tympanic membrane for insertion of a tube through the tympanic membrane. This procedure relieves the painful pressure inside the middle ear (resulting from the infection) by allowing fluid to drain from the ear. However, unless the bacteria in the middle ear are treated, the infection can continue after cleaning the external auditory canal and after introducing a tube through the tympanic membrane.

As explained earlier with respect to general wounds, systemic antibiotics are not necessarily the first choice of treatment because of the complications of associated with systemic antibiotics (e.g., nausea, gastrointestinal upset) as well as the possibility of incurring a superinfection when the infection results from a resistant form of bacteria or pathogenic microflora. Of course, it is also generally advantageous to avoid surgical intervention on the tympanic membrane whenever possible.

It is desirable to use a non-contact, non-surgical intervention method of killing bacteria and drug delivery. As shown in FIG. 21, an ear 130 includes an inner surface 132 of an external auditory canal 134. A tympanic membrane 136 is located at the most interior portion of the canal 134. A middle ear 138, including an incus 140, malleus 142, and a stapes 144, is located adjacent to and just interior of the tympanic membrane. Bacteria is typically located in the region of the middle ear 138.

Killing bacteria in the ear using the method of the present invention includes providing an antibiotic fluid 52 within fluid reservoir 38 of the sprayer 16. The sprayer 16 is positioned such that the free end surface 75 of the transducer tip 74 is aligned with the external auditory canal 134 of the ear 130 so that the long axis of the transducer tip 74 is substantially parallel with the long axis of the external auditory canal 134. A directed spray 80 of the antibiotic is created and forcefully projected from the free end surface 75 in the manner described for the method of the present invention in association with FIGS. 2-4. This method includes the step of providing a source of low frequency ultrasonic waves and the step of delivering the liquid 46 to the free end surface 75 of the ultrasonic transducer tip 74. The method further includes orienting the spray 80 of antibiotics to enter the ear canal 134 and strike the surfaces 132 along the auditory canal 134 as well as the surface of the tympanic membrane 136. The antibiotic spray particles 82 are propelled by the ultrasonic waves emanating from the free end surface 75 and the spray particles 82 act as a medium (in combination with the ambient air) for carrying the ultrasonic waves into the tissue of the auditory canal 134 and for penetration into the tympanic membrane 136 up to 1 millimeter in depth. A continuous spray can be applied within the external auditory canal 134 for about 30 to 60 seconds and up to five minutes, or for whatever duration and frequency deemed necessary by a user of the device. As an example, this treatment can be given once a day for several days in a row (e.g., three days to two weeks). A distance of separation of about 1 to 10 centimeters can be preferably maintained between the tympanic membrane 136 and the free end surface 75 of the transducer tip 74 during the step of orienting the spray 80 onto the respective tissue surfaces.

The method of the present invention for killing bacteria within an ear enjoys the same advantages and effects as described earlier in association with FIGS. 2-4 for the general method of the present invention for killing bacteria on a wound surface or non-biological surface. In particular, amongst

other advantages, the insonified (i.e., highly activated) antibiotics of liquid 52 of the particle spray 80 and the low frequency ultrasonic waves penetrate the tympanic membrane 136 and surface 132 of the external auditory canal 134 to actively disrupt and destroy the bacteria cells on and within the tissue.

In addition, all of the modifications of the method of the present invention of killing bacteria as described in association with FIGS. 2-20 can be selectively incorporated into the method of the present invention of killing bacteria within an ear. This includes modifications of the free end surface of the transducer tip, of delivering the liquid, and of modifying the frequency of ultrasonic waves provided at the free end surface of the transducer tip.

Although the method of treating an ear was described using an antibiotic, many other medicines can be used in the method of the present invention.

The method can be used to kill bacteria on other surfaces of the body including the nose, eyes, mouth, and vagina.

3. Example 1: Experimental Animal Testing

Before introducing the method of the present invention into human clinical testing, a series of experiments was performed on rabbits at the Baku Institute of Traumatology and Orthopedics in Baku, Azerbajan. The experiments comprised making identical wounds on identical parts of rabbits with a scalpel and then treating the wounds with the method of the present invention. One rabbit was retained as a control, and other series of rabbits were treated with various regiments of ultrasound atomization of antibiotics.

The study was performed in accordance with the experimental protocol established by the Ministry of Health of the U.S.S.R. in Moscow, Russia. The Protocol No. 10 11-10 (established January 17, 1983) for Extraction and Identification of Pseudomonas Aeruginosa Culture From Clinical Bioptate was followed.

The method of the present invention was applied using a frequency of ultrasonic waves of 26.5 +/- 1 kiloHertz. This frequency is thought to maximize cavitational effects that disrupt bacterial cells. The ultrasonic generator 12 was operated to test ultrasonic wave oscillation amplitudes of 10, 30, 60, 80 and 100 microns. Treatment times included durations of continuous spraying for 30 seconds, 60 seconds, 3 minutes, 5 minutes, and 10 minutes.

Histologic analyses of the wounds on the rabbits was performed in the Laboratory of Histology and Morphology of Baku Institute of Traumatology and Orthopedics. The analyses showed no remarkable deviations in the ultrasonically treated wounds as compared to the control wound. 18 rabbits were included in the experimental group.

Next, morphological and microbiological analyses were conducted to make a combined scientific study of the therapeutic effect of low-frequency ultrasound as a prophylactic for bacteria growth.

Purulent infected wounds with varying area and depth were modeled in the animals in the upper third of the thigh. Treatment was conducted by the generally accepted methods in the control group. The animals in the control group received massive doses of broad-spectrum antibiotics and sulfanilamides. Oxidants and antimicrobial preparations were applied locally to the infected surface. The infected surface was also regularly washed with hydrogen peroxide, furacillin, permanganate, and was sprinkled with antibiotics, novamine, baliz-2 and other conventional preparations. Sterile dressings were applied and the wound was drained.

In another series of experiments using the method of the present invention, the same medicinal preparations were used as for the control group, except that the medicinal preparations were applied to the surface of the wound in the "insonified" aerosol state using the method of the present invention. In each series of experiments there were no less than 30 experimental rats. The

number of ultrasound procedures, exposures of the treated wound surfaces, and system of preparations for external application were selected in each series considering the status of the suppurative inflammatory process. Morphologic, histochemical and microbiological monitoring of the condition of the wound focus was performed in parallel.

In the control series of experiments, there was active destruction of the injured tissue and cellular immunity was clearly evident in 60-70% of the experimental animals. In 30-40% of cases, the purulent-inflammatory process extended into the underlying tissue with subsequent generalization (i.e., spread to other tissues) of the infectious process and death of the experimental animals. In the surviving animals of the control series of experiments, the proliferative regenerative process in the tissue was weak and final healing of the wound occurred at 25 to 30 days following creation of the model wound and the beginning of treatment by traditional methods.

In the series of experiments with treated with the method of the present invention, the purulent infected wound was treated with a liquid aerosol of the medicinal preparations (oxidants, antibiotics, antimicrobials). The medications were applied, using the method of the present invention, to the wound surfaces twice per day with a distance of separation between the transducer tip and the wound surface being 4 to 7 centimeters. The duration of treatment time was 30-60 seconds. In parallel, microbial flora were obtained from the wound and histologic monitoring of the regenerative processes was performed. Biochemical and cytochemical monitoring of the immune status of the peripheral blood of the experimental animals was also performed.

The studies showed that treatment of the bacteria laden wound surface with preparations insonified using the method of the present invention was effective in accelerating the process of regeneration, isolating the purulent inflammatory focus, rapidly removing wound detritus and promoting final epithelialization of the wound surface. In studying the effect of the insonified

antiseptics and antibiotics in the method of the present invention, it was determined that the application of low-frequency ultrasound gives the antiseptics and antibiotics additional biological activity and effectively suppresses the viability of pathogenic flora in the purulent inflammatory focus. In the experiments, the entire process (from the moment of creation of the model purulent inflammatory focus to its complete healing) lasted no more than 12 to 15 days under conditions of regular treatment of the wound area with the insonified preparations in the method of the present invention.

This time period (12 to 15 days) includes the time of cleansing of the wound of tissue detritus, regeneration of the juvenile connective tissue and epithelialization of the wound surface. Thus, the time required for complete healing of the infected wound was reduced by a factor of 2-2.5 in comparison with the control series of experiments, in which the treatment of the purulent inflammatory focus was performed by traditional methods. Microbiological monitoring of the condition of the pathogenic flora (Streptococcus aureus, Pseudomonas pyocyanea, Bacillus coli, etc.) screened from the purulent inflammatory focus showed that the preparations insonified with low-frequency ultrasound in the method of the present invention suppress their virulence, i.e., their ability to reproduce.

4. Example 2: Clinical Human Tests

After the successful trials within animal testing, the method of treatment of the present invention was applied to human patients having purulent infected wounds.

Treatment of wounds using the method of the present invention was performed on patients with various diagnoses, such as extensive bacteria laden infected wounds of the lower leg, foot and hand, and also wounds following trauma or surgery which failed to heal over a considerable time.

Treatment of purulent infected wounds was performed using the method of the present invention as previously described in association with

FIGS. 2-4. The duration of treatment was 30 seconds to five minutes and a course of treatment consisted of up to 5 sessions, depending on the condition of the wound and the progress of the healing process, as determined by a physician using the method.

The results were evaluated on the basis of the clinical and bacteriological data (see Table 1.1). The bacteriological analysis was performed before and after each ultrasonic treatment session of a purulent wound. The qualitative and quantitative composition of the microflora was determined. The quantitative composition of the microflora (number of microbial cells in 1 g of tissue) was determined in a bioptate (i.e., biopsy) obtained from the wound of a patient.

Before ultrasonic treatment of infected wounds of trauma patients, a high degree of bacteriological contamination of the wounds was observed (1 x 10^5 to 1 x 10^9 microbial cells per gram of tissue). Treatment of the wound using the method of the present invention for several seconds yielded no significant reduction in microflora, but did cause mechanical cleansing of the wound of tissue detritus and blood clots. However, repeated treatment of the wound using the method of the present invention for longer durations (e.g., 30 seconds or more) reduced bacterial contamination to about 1 x 10^4 to 1 x 10^5 microbial cells per gram of tissue.

The results of determination of the qualitative and quantitative composition of the microflora in the wounds are presented in Table 4.1. As seen in the table, ultrasound treatment using the method of the present invention was applied to purulent wounds having post-traumatic osteomyelitis developing after open fractures. The method of the present invention was applied to purulent wounds on patients during changing of dressings. The medicines used included 0.2% solutions of chlorhexine, or an antibiotic to which the microflora of the wound were sensitive. The entire surface of the wound was treated, as well as the surface surrounding a fistula. One to five treatments were applied,

depending on the size, nature of the wound and the purulent discharge. The volume of solution used varied between 50 to 100 ml of solution.

Microbiological study of purulent wound bioptates taken from the wounds established that, prior to ultrasound treatment with the method of the present invention, the following bacteria were found in the purulent wound tissue of three patients: Staphylococcus (St. aureus and St. epidermidis) in monoculture, gram-negative flora (Klebsiella, Pseudomonas pyocyanea and E. coli), and gram-positive diplococci. Microbiological study of the purulent foci of 7 patients yielded Ps. aeruginosa, both in monoculture and in association with staphylococci, gram-positive diplococci and Klebsiella. Microbiological study of the infected wounds of the remaining 3 patients yielded gram-positive diplococci and E. coli in monoculture.

Before treatment was initiated, the total number of bacteria per gram of tissue taken from deep wounds was 1×10^6 to 1×10^9 microbes in 13 patients, which is higher than the critical level. In one patient, 1×10^5 microbes (within the critical level) were found in the wound tissue and in another patient, 1×10^4 microbes were found, which is below the critical level.

In the process of combined treatment (antitoxication, antiseptic-antibiotic, general strengthening and other therapy) of purulent wound patients using the method of the present invention, the bacteriological analysis showed that in 4 cases, the gram-positive diplococci found prior to application of ultrasound by the method of the present invention were absent in the bacteriological samples after treatment of the wound (case histories No. 8064, 10816, 1202, 9173). In another case, a group of pathogens was found (Staphylococcus St. aureus and Pseudomonas aeruginosa) in samples of purulent material prior to treatment and that, after treatment with the method of the present invention, bacteriological studies continued to produce Ps. aeruginosa. This may be related to its high resistance to antibiotics and antiseptics (case

history No. 10816). The samples were negative. These results indicate little change in the qualitative composition of the wound microflora.

Nevertheless, the quantitative composition of the microflora in 15 infected patients was compared before and during treatment with the method of the present invention. It was found that prior to treatment, each gram of bioptate of wound tissue contained from 1.0×10^6 to 1.0×10^9 microbial cells. However, after treatment with the method of the present invention, the number of microflora in the bioptate of the purulent wounds (with combined treatment) dropped to 1.0×10^5, or less than the critical threshold in 67% of the total number of patients (in 10 cases). In the remaining 33% of the total number of patients (in 5 cases), the number of microflora fell to 1.0×10^6 to 1×10^7 as found in the bioptates of the wound tissue. However, the latter result (in the 33% of patients) does not mean ineffectiveness against the bacterial population of the wound. Rather, with respect to the number of bacteria contained in one gram of tissue, there was a reduction in the number of microflora by one to three orders of magnitude after ultrasound treatment of the wounds.

The microbiological study data was consonant with the observed clinical course of the wound process. As noted in the treating physicians daily case histories of the patients, one to three days after the first treatment with the method of the present invention, the wounds were cleansed of necrotic tissue, edema was reduced, discharges were slight or stopped entirely, and granulation was seen. After the completion of the combined treatment of infected wounds with the method of the present invention and before release of the patients, the wounds were clean, decreased in size, rapid epithelialization was under way, fistulas had closed, and there was no discharge.

One-time treatment of the wound with the method of the present invention for 1-5 minutes yielded no significant reduction in the number of microflora per gram of tissue, but did cause mechanical cleansing of the wound of detritus and clots of blood and removal of necrotic masses. About 5-6 hours

following treatment, the patients reported mild itching in the wound and surrounding area. After repeated treatment, the wound was further cleaned of fibrinous-purulent encrustation and necrotic tissue. Bacterial contamination was reduced by 2-6 orders of magnitude. With one or two treatments of low-frequency ultrasound using the method of the present invention, the wounds became clean and active granulation was observed. Subsequent treatment of purulent wounds with the method of the present invention also facilitated appearance of strong granulation, a reduction in inflammatory infiltrate and complete healing of the wound. It was not possible to collect a bioptate from the depth of the wound after the 4th or 5th treatment because the healing of the wound had progressed sufficiently and the wound was covered by granulation tissue.

Accordingly to the data in Table 4.1, in all cases of treatment with the method of the present invention for one to three sessions, there was a decrease in the bacterial population to or below the critical level, which indicates the process of healing of the wound.

For example, the results of the clinical course of the wound process in patient A. R. V-a, 59, case history No. 1133, with combined treatment before and after treatment with the method of the present invention, are worth noting. Patient number 5 (A. R. V-a) entered the Clinical Emergency Hospital with the following diagnosis: "Extensive scalped wound of the lower third of the right calf, posterior surface and foot, with compression of the soft tissue of the calf. Marginal fracture of the malleolus, no displacement." This trauma was received by the patient in an automobile accident. The wound was infected and the size of the wound surface was 2010 cm^2. Before treatment with the method of the present invention, the bioptate of the extensive purulent wound yielded Pseudomonas aeruginosa having 7.2×10^6 microbe cells per gram of tissue.

In the process of combined treatment including treatment with the method of the present invention combined with kanamycin, Pseudomonas aeruginosa remained but its quantity per gram of bioptate dropped to 24 x 10^4 microbe cells. This level is below the critical level by 2 orders of magnitude. Clinically, by the third day after treatment with the method of the present invention, the wound was cleansed of purulent-necrotic masses, swelling was decreased, mild granulation had started. By the end of low-frequency ultrasound treatment with the method of the present invention, purulent discharge was stopped, clear granulation was evident, and the wound had decreased in size. After complete healing of the wound patient V-a received plastic surgery of the skin.

Qualitative determination of the microflora before and after treatment with the method of the present invention in the combined treatment of the purulent wounds was performed on 17 patients. The purulent material was collected from the wounds by tampon. The results of microbiological studies are presented in Table 4.2. The patients with infected wounds of the extremities also received the same treatment. There were one to four treatments of the wounds using the method of the present invention. Antibiotics or antiseptics to which the microbes were sensitive were applied with the method.

The microbiological studies showed that prior to treatment with the method of the present invention with combined treatment of purulent wounds, the bacteria Proteus (4), Klebsiella (2), Ps. aeruginosa (1), Staphylococcus St. epidermidis (2) and gram-positive diplococci were present in monocultures. In the remaining cases, microflora were found in association.

In the process of combined treatment including treatment of the method of the present invention, the wounds were cleansed of pus and necrotic masses, discharges decreased. In the bacteriological analysis, the microflora were found to remain present and to basically have the same qualitative composition as earlier. Only in two cases were associations of cultures (gram-

positive diplococci and Ps. aeruginosa) replaced by monocultures of Ps. aeruginosa (case history No. 6678 and No. 4441).

However, although the cultures continued to be produced from the infected wound surface with combined treatment including treatment with the method of the present invention, the clinical course of the wound process was favorable. After one to three days of treatment, the surgeons noted a decrease in the discharge and size of the wounds and noted clear granulation with a tendency toward epithelialization. Only in one case did the purulent discharge continue, although to a significantly lesser extent than before treatment (case history No. 1633).

The results of the studies suggest that treatment using the method of the present invention in combination with sensitive antibiotics or antiseptics has a direct influence on the pyogenic wound microflora. This is observed in the reduced quantitative composition of the microbes and the beginning of active healing. The physical effects of the ultrasound application of the method of the present invention may cause a change in the bacteria cell membrane, which leads to rapid penetration of the medication and a decrease in the virulent properties of the bacteria or microbe. Therefore, even though the bacteria or microflora may continue to be cultured in the process of treatment, the microflora may be less virulent and more susceptible to the forces of the microorganism since the process of wound healing is intensive.

Thus, the studies of the method of the present invention on wounds of the extremities dictates this method be given a positive evaluation as a part of a combination for prevention and treatment of wound infection with open injuries of the extremities.

Regarding control patients, ten patients did not receive ultrasonic treatment with the method of the present invention of purulent wounds. They were treated by conventional methods. The results of the investigation of bioptates of purulent wounds of these patients are presented in Table 4.3.

Analysis of the data obtained from bioptates of the wound tissue demonstrates that, before treatment and in the process of treatment, the qualitative composition of the microflora did not change.

Samples of purulent materials of the wounds yielded Staphylococcus (St. aureus, St. epidermidis) Pseudomonas.aeruginosa, E. coli and others in monoculture. The number of microbes per gram of tissue in 9 patients was 1×10^6 to 1×10^8 cells, higher than the critical level. The content of microbes per gram of tissue dropped by only 1-2 orders of magnitude in the process of treatment.

Regarding the types and prevalence of bacteria found in the experimental group, bacteriological study of the bioptates and cultures in patients with purulent-inflammatory processes before use of ultrasound in the method of the present invention showed that the leaders among pathogens in the purulent foci were staphylococci (St. aureus and St. epidermidis), representing 31.6% (18) cultures, Pseudomonas aeruginosa, representing 26.3% (15) cultures, while 42.1% (24) cultures consisted of accompanying microflora (gram-positive diplococci, gram-negative bacilli, diphtheroids, etc.).

The purulent wounds of 42 patients prior to treatment yielded 57 strains of microorganisms. In 37% (3) of the cultures Staphylococcus aureus appeared in monoculture and in 62% (5) Staphylococcus aureus appeared in association with other microorganisms. Staphylococcus epidermidis was cultured in 60% (6) of the cultures in monoculture and in 40% (4) in association with other microflora including: Staphylococcus aureus in 17% (10) cultures, Pseudomonas aeruginosa in 40% (6) cultures in monoculture and in 60% (9) in associations.

The bacteriological studies showed that there is a tendency for increasing appearance of Staphylococcus aureus and Pseudomonas aeruginosa in associations with accompanying microflora and increasing yield of Staphylococcus epidermidis in monoculture.

Antibiotic-response diagrams were produced for the microorganisms found with 20 antibiotics: neomycin, heptamycin, rifampicin, penicillin, ampicillin, erythromycin, monomycin, polymyxin, streptomycin, lincomycin, carbenicillin, kanamycin, methicillin, oxacillin, oleandomycin, tetracycline, fusidine, levomycetin, ristamycin and dococycline.

The antibiotic-response diagrams showed that thirteen strains of microbes were monoresistent (sensitive to a single antibiotic), amounting to 22% of the total. Seven strains were sensitive to two antibiotics (12%), four strains were sensitive to three antibiotics (17%), two strains each were sensitive to six and eight antibiotics (3% each), and 1 strain each of microbes showed sensitivity to 4, 5, 10, 11, 12 and 18 antibiotics (1% each).

Among the strains obtained from the purulent wounds, 21 strains of microorganisms were sensitive to 20 antibiotics, which amount to 37%.

To estimate the economic effectiveness of the use of ultrasonic treatment of purulent wounds, we undertook a comparative computation of patient bed-days. Data on the time spent by patients in the hospital were taken from the case histories. The computation of bed-days of patients who received ultrasonic treatment in combined treatment of purulent wounds was performed in comparison with the bed-days of patients treated by generally accepted methods. It was noted that, on average, treatment of patients with the method of the present invention resulted in a reduction of time spent in the hospital by 3.8 to 4.0 bed days. This can result in cost savings and a reduction of lost work days.

5. Example 3: Photographs of Bacteria Treated with the Method of the Present Invention

FIG. 26 illustrates a healthy bacteria cell, Pseudomonas Aeruginosa, prior to treatment with the method of the present invention. The photograph of FIG. 26 is an image of a bacteria cell at 50,000 times magnification obtained with a scanning electron microscope. The bacteria cell

was taken from a bioptate of a wound of a patient and then mounted on a viewing medium. This single bacteria cell was separated from other bacteria in the bioptate of the wound. As seen in FIG. 26, the bacteria cell includes a body portion with whiplike organelles extending from the body portion for securing the bacteria cell to a surface, e.g., tissue.

This bacteria cell was treated with the method of the present invention in the manner previously described in association with FIGS. 2-4. Upon treatment for about fifteen seconds with a distance of about 10 centimeters between the bacteria and the free end surface of the ultrasonic transducer of the sprayer, the bacteria were physically changed to the state shown in FIG. 27. FIG. 27 illustrates that the bacteria cell (at 50,000 times magnification) has lost its organelles, has begun to bulge, and has become much shorter and wider after treatment with the method of the present invention.

The bacteria cell was treated about another fifteen seconds with the method of the present invention with the result shown in FIG. 28 (50,000 times magnification). In FIG. 28, the bacteria cell has shrunk even further. More importantly, the bulges shown in FIG. 27 have been punctured such that the contents of the cell are forced outside the cell causing death of the bacteria cell. As part of this destruction, the cell wall has separated from the contents of the cell also effectively killing the cell.

FIG. 29 illustrates a colony of bacteria cells at 15,000 times magnification (by a scanning electron microscope) after treatment with the method of the present invention. The duration of treatment was approximately 60 seconds. Each cell in FIG. 29 has reached the state of puncture and expulsion of some cell contents as well as separation of the cell wall from the cell contents.

Table 4.1.--Determination of Qualitative and Quantitative Composition of Microflora of Purulent Wounds of Traumatology Patients Subjected to Ultrasound Treatment in Combination with Antibiotics or Antiseptics

No.	Case No.	Name	Diagnosis	Complication	Type and Size of Wound before Sonication	Before Treatment	
						Cultured	Microbes/g
1	8064	R.M.G-v,8	Severe open trauma of right hand with crushing of all fingers	Infected wound of right hand	Wound on right hand measures 4x20 cm	St. aureus, Ps. aeruginosa, klebsiella, gram(+) diplococci	1.062×10^3
2	6898	D.U.T-n,32	Closed transverse fracture of middle third of right femur with displacement of fragments. Extensive peeling of skin on inner surface of upper third of thigh and left calf	Infected wound of left calf	Wound measures 6x8 cm	St. aureus, Ps. aeruginosa	1.0×10^9
3	9781	I.P.K-e,24	Extensive crushing wound of right upper extremity	Infected wound of right forearm	Scalping wound from upper third of right shoulder to radiocarpal joint. Skin 5-8 cm above ulna exposed. Left upper extremity from middle third of the shoulder to middle third of the forearm		3.3×10^8
4	9820	V.Z.N-v,34	Crushing wound of left upper extremity with open splinter fracture of the shoulder condyle	Infected wound of the left upper extremity	Left upper extremity from middle third of the shoulder to middle third of the forearm	Ps. aeruginosa	1.10×10^7

5	1133	A.R.V-a,59	Extensive scalped wound lower third of right shin, posterior surface and foot with compression of soft tissue. Marginal fracture of ankle, no displacement	Extensive infected wound of right shin and foot	Wound on posterior surface lower third right shin and foot measures 2x10 cm	St. Epidermidis	$7.2x10^6$
6	2520	F.G.A-v,22	Laceration and contusion of left foot with peeling of skin on sole	Infected wound of left foot	In area of metatarsal bones of foot with inferior surface of left foot	St. aureus, Ps. aeruginosa	$3.1x10^6$
7	10826	I.R.R-v,53	Open fracture in left ankle, crushing fracture of left calcaneus	Infected wound of left foot	Starting posterior to ankle up to forepart in horizontal position	gram(+) diplococci	$1.1x10^6$
8	3845	L.M.K-v,37	Penetrating laceration-contusion of lower third, left thigh	Infected wound of left thigh	On medial and exterior surface of thigh, 12x4 cm and 3x4 cm	gram(+) diplococci	$5.6x10^4$
9	4719	S.K.S-v,51	Aggravated chronic osteomyelitis of left thigh with functional fistula	—	In lower third of left thigh outer and inner surfaces of thigh, fistula with purulent discharge	St. epidermidis	$2.4x10^7$
10	3200	I.N.M-v,68	Residual problem after contusion of left foot, upper third of left shoulder. Extensive necrosis of skin of left arm	Infected wound of left foot	On left foot on exterior surface of heel area, wound 12x18 cm	E. coli	$1.8x10^6$
11	4636	A.A.P-v,49	Chronic osteomyelitis of metatarsal bones of left foot	—	Modest discharge from fistulas	St. epidermidis E. coli	$7.3x10^6$
12	4592	V.B.D-v	Chronic osteomyelitis of bones of left foot with functional fistula after arthrodesis operation	—	Purulent discharge from sole of left foot	St. aureus	$5.8x10^6$

13	1202	A.A.S-n,53	Open splinter fracture of terminal phalanxes II-III-IV of right hand with crushing of soft tissue	Infected wound of fingers of right hand	In area of fingers II-III-IV of right hand, extensive gram(+) diplococci, Ps. aeruginosa	1.8×10^7	
14	4052	S.M.A-v,34	Aggravation of chronic osteomyelitis of lateral malleolus and left talus	—	Purulent discharge from fistula in area of left medial malleolus	St. aureus, Klebsiella	2.3×10^5
15	9173	S.A.I-a,35	Crushing of right hand with open fractures of II-III-IV metacarpal bones and proximal phalanxes Infected wound of right hand	Extensive deep wound on internal and posterior surface of right hand	Gram(+) diplococci, Klebsiella	5.0×10^6	

Table 4.1.--Continued (Right half)

No.	No. of Treatments with Antibiotic or Antiseptic	In Process of Treatment		Nature of Wound after First Treatment	Nature of Wound after Last Treatment	Bed-Days
		Cultured	Microbes/g			
1	5 times with monomycin	St. aureus, Ps. aeruginosa, Klebsiella	2.54×10^7	Wound clean, healing	Wound clean, size decreasing	118
2	4 times with monomycin	St. aureus, Ps. aeruginosa	3.4×10^4	Cleansed of necrotic tissue and pus, slight purulent discharge	Rapid epithelization and decreasing purulent discharge	244
3	3 times with penicillin	Ps. aeruginosa	6.9×10^3	Cleansed of necrotic tissue	Wound clean, no discharge	58
4	4 times with lornexidine	Ps. aeruginosa	3.2×10^1	Cleansed of purulent-necrotic masses	Wound clean, granulation	120
5	4 times with kanamycin	St. epidermidis	2.4×10^4	Cleansing from purulent-necrotic masses, slight granulation	Decrease in size, complete cleansing of purulent encrustation	80
6	3 times with monomycin	Ps. aeruginosa	8.0×10^6	Edema moderating, discharge slight	Wound clean, covered with epithelium	74
7	2 times with ampicillin	No growth of microbes	0	Discharge stopped	Wound clean	120
8	3 times with Chlorohexidine	Gram(+) diplococci	4.2×10^1	Wound cleansed of necrotic masses	Wound clean, granulation occurring	24
9	1 time with ampicillin	St. epidermidis	3.6×10^6	Discharge stopped	Wound healed	19
10	1 time with Kanamycin	E. coli	7.5×10^6	Granulation noted	Wound clean	91

11	1 time with heptamycin	St. epidermidis, E. coli	3.0×10^4	Discharge reduced	Wound clean, no discharge	54
12	1 time with oxacillin	St. aureus	3.6×10^5	Discharge significantly reduced	Wound clean, discharge stopped	63
13	3 times with kanamycin, oxacillin	Ps. aeruginosa	1.0×10^5	Wound clean, epithelization in process	Wound healed, completely covered with epithelium	65
14	? times with kanamycin,	St. aureus, Klebsiella	1.0×10^5	Discharge stopped	Fistula fully closed, no discharge	60
15	3 times with penicillin	Ps. aeruginosa, Klebsiella	3.0×10^5	Wound cleansed of necrotic tissue	Size of wound reduced, epithelization in process	73

Table 4.2.--Qualitative Composition of Microflora of Purulent Wounds of Trauma Patients Subjected to Ultrasound Treatment

No.	Case History	Name, Age	Diagnosis	Complication	Nature and Size of Wound before Ultrasound	Cultured before Ultrasound
1	2385	Z.M.M-v, 54	Open shattered fracture of metacarpal bones III-IV-V of left foot	Infected wound of left foot	Extensive deep wound on anterior surface of left foot from margin at base of III phalanx	Ps. aeruginosa
2	1872	E.M.R-v, 43	Traumatic separation of both thighs, acute hemorrhage, traumatic shock stage III-IV	Infected wound of right and left stumps and left thigh	Purulent discharge in lateral surface of left thigh and both stumps	E. coli
3	1157	V.V.B-n, 28	Traumatic amputation in middle third of right tibia, shock stage II, dermal defect of stump	Infected wound of right stump	Purulent discharge from stump wound lower third right calf	Ps. aeruginosa, St. aureus
4	1601	B.G.R-n, 46	Traumatic separation of lower third left calf; right great toe crushed toe V of right foot	Infected wound of left calf stump	Purulent discharge from stump wound, middle third of left calf	Ps. aeruginosa, St. aureus
5	1633	V.N.N-v, 18	Fracture of middle third of right tibia, grown together, with metal pin, chronic osteomyelitis with func. fistula	--	Purulent discharge from fistula middle third of right tibia	St. epidermidis
6	6678	R.V.M-a, 60	Closed fracture of head of right radius, extensive infected laceration in area of elbow with significant skin defect	Infected wound of upper extremity	Extensive wound in area of elbow	Gram (+) diplococci, Ps. aeruginosa
7	1469	Kh.A.B-a	Extensive contusion-scalped wound of lower third of left calf, ankle and foot on right side. Open fracture of lateral malleolus	Infected wound of left calf and foot	Wound on posterior surface of ankle, starting at lower third of calf and ending in middle of foot. Skin flaps fully separated	Ps. aeruginosa, St. epidermidis
8	715	N.N.G-v, 57	Closed splinter fracture of middle third of left tibia	Infected bedsore	In area of sacrum and right heel	Pr. vulgaris

9	11206	A.M.A-v, 23	Infected wound of right hand	--	Posterior surface of finger I, wound 0.5 cm	Gram(-) diplococci
10	3280	Ya.G.S-i, 60	Chronic osteomyelitis of right tibia with functional fistula and extensive ulcerative wound in lower third of right calf	--	Lower third of right calf, wound 10x6 cm with purulent discharge	S. epidermidis, Gram(-) diplococci
11	10850	K.M.N-v, 56	Status after dermoplasty, finger I of right hand with scalped wound, skin defect of bone phalanx. Osteomyelitis of phalanx	--	Posterior surface of finger I of right hand, wound 0.2x0.3 cm	St. epidermidis
12	4605	E.Z.B-v, 67	Open dislocation of right medial bone, extensive contusion in area of right ankle	Infected wound of right ankle	Laceration-contusion of external surface of ankle 12x4 cm	Klebsiella, E. cloacae
13	4792	G.A.Ya-v, 53	Round laceration-contusion wound of lower third of left forearm with damage to bones of forearm and radiocarpal joint	Infected wound of stump, lower third of shoulder joint	Wound of stump size of kopek coin	Pr. mirabilis
14	4441	Yu.S.N-v	Closed fracture of primary phalanxes of fingers III-IV-V of left foot, contusion of left ankle	Infected wound of left ankle	In area of Achilles tendon wound 10x5 cm	Gram (+) diplococci, Ps. aeruginosa
15	3274	L.S.N-v, 64	Extensive infected radial ulcer of skin in suprascapular area	--	Right suprascapular area purulent wound 10x6 cm	Klebsiella
16	5592	N.K.Apv, 65	Open infected fracture of right radius with displacement, extensive infected wound of right radiocarpal joint	--	Lower third of left forearm, wound 8x10 cm	Pr. mirabilis
17	5255	G.A.K-v, 33	Closed multiple-fragment fracture of right femur	Infected wound of right femur	--	Pr. mirabilis

Table 4.2.--Continued (Right side)

No.	Ultrasound Treatments with Antibiotic or Antiseptic	Culture from Wound During Treatment	Wound after Treatment, 1 Day or More (up to 3 Days)	Nature of Wound after Last Ultrasound Treatment	Bed-Days
1	3 times with heptamycin	Ps. aeruginosa	Moderate serous discharge noted	Wound clean, granulation in process, healing	43
2	3 times with polymyxin	E. coli	Discharge significantly reduced, epithelization occurring	Wound clean	45
3	3 times with polymyxin	Ps. aeruginosa, St. aureus	Wound clean, granulation occurring	Rich granulation, good epithelization	47
4	3 times with polymyxin	Ps. aeruginosa, St. aureus	Wound clean, granulation occurring	Wound healed, fully covered by epithelium	18
5	4 times with erythromycin	St. epidermidis	Discharge significantly reduced	Fistula tightens, but discharge still present	79
6	4 times with polymyxin	Ps. aeruginosa	Wound clean, discharge decreases	Wound healed	67
7	3 times with ampicillin	Ps. aeruginosa, St. epidermidis	Wound clean	Wound clean, scarring occurring	101
8	3 times with penicillin	Pr. vulgaris	Cleansed of pus and necrotic masses	Bedsores healed	72
9	3 times with heptamycin	Ps. aeruginosa	Modest serous discharge	Wound clean, granulation occurring, healing	43
10	3 times with polymyxin	E. coli	Discharge significantly reduced, epithelization in process	Wounds clean	45
11	3 times with Polymyxin	Ps. aeruginosa, St. aureus	Wound clean, granulation in process	Rich granulation, good epithelization	47
12	3 times with polymyxin	Ps. aeruginosa, St. aureus	Wound clean, granulation in process	Wound healed, completely covered with epithelium	18

13	2 times with chlorohexidine	Pr. mirabilis	Wound shrinking, discharge stopped	Wound clean, granulation occurring	54
14	3 times with chlorohexadine, heptamycin	Ps. aeruginosa	Wound clean	Wound healing, clear granulation under way	80
15	2 times with heptamycin	Klebsiella	Wound decreasing in size	Wound healing, clear granulation under way	111
16	2 times with chlorohexidine	Pr. mirabilis	Discharge decreased, wound shrinking	Wound healed	40
17	1 time with chlorohexidine	Pr. mirabilis	Discharge decreased, wound shrinking	Wound healed	26

Table 4.3.--Microflora Taken from Trauma Patients not Treated with Ultrasound

No.	Case History	Name, Age	Diagnosis	Complication	Type and Size of Wound	Before Treatment		During Treatment		Bed-Days
						Microflora	Microbes/g	Microflora	Microbes/g	
1	9018	M.G.K-a,70	Closed fracture of radius, open fracture of lower third of left femur with displacement of fragments	Infected wound of left femur	Wound in area of outer surface of femur 4 cm	Gram(+) diplococci	$1.0x10^7$	Gram(+) diplococci	$1.0x10^7$	
2	6470	S.I.G-v,70	Trophic ulcer, chronic osteomyelitis of left tibia	—	Purulent discharge from fistula or left calf	St. epidermidis	$1.0x10^7$	St. epidermidis	$2.3x10^8$	
3	330	N.S.P-ya,55	Closed multiple fracture of left ribs, scapula, multiple hemorrhages of thorax, femur	Infected wound of left thigh	Purulent discharge from wound in left thigh	St. epidermidis	$3.5x10^7$	St. epidermidis	$1.0.x10^7$	
4	9953	A.A.M-v,72	Chronic osteomyelitis of proximal end of left tibia with func. fistula	—	In upper third of right femur is func. fistula		$8.1x10^3$		$4.2x10^3$	47
5	5828	N.A.P-v,60	Traumatic amputation of fingers III-IV of right hand and fracture of terminal phalanx of finger V	Infected wound of right hand	Discharge from interior surface of finger II and on palmar surface of finger III		$1.0x10^8$		$1.0x10^7$	43
6	7374	N.A.P-v,60	Chronic osteomyelitis of finger III of right hand with multiple fistulas in aggravation stage and difficulty moving finger III of that hand	—	On right hand in area of finger III infected wound with multiple fistulas in aggravation		$2.7x10^4$		$1.0x10^4$	87

7	9887	A.G.S-n,17	Closed fracture of middle third of bones in left forearm with ulnar nerve displacement and contusion	Infected wound of left forearm	Extensive purulent wound on anterior surface of middle third of left forearm		4.9×10^7		2.6×10^3	40	
8	4636	Kh.V.B-a,78	Glove denudation of the right side with crushing of soft tissues of sole surface	Infected wound of the right foot	Extensive laceration and contusion of the lower third of the calf, posterior and anterior surfaces to base of toes	Diphtheroids	4.5×10^6	Diphtheroids	4.5×10^3	167	
9	117	D.F.I-v,29	Open fracture of lower third of left ulna with displacement. Crushing wound of left forearm with damage to extensor tendons and soft tissues	Infected wound of left forearm	In anterior external surface of left forearm crushing wound 8x15 cm	Ps. aeruginosa	1.0×10^6	Ps. aeruginosa	2.5×10^4	57	
10	1172	A.E.A-v,85	Closed oblique fracture of upper third of right humerus with separation of greater tubercle, dislocation of right shoulder	Infected wound of right humerus	Postoperative wound in upper third of right humerus, discharge from fistula	E. coli	2.3×10^6	E. coli	1.0×10^6	124	

Although the present invention has been described with reference to preferred embodiments, workers skilled in the art will recognize that changes may be made in form and detail without departing from the spirit and scope of the invention.

5

WHAT IS CLAIMED IS:

1. A method of spraying a surface comprising:

producing a particle spray of liquid particles produced by contact of liquid with an ultrasonic transducer operating at a frequency of between about 16 and 200 kilohertz; and

directing the particle spray onto the surface while maintaining the transducer at a distance of at least about 0.5 centimeters from the surface.

2. The method of claim 1 wherein the producing step includes the liquid contacting a free end surface of the ultrasonic transducer to produce the spray.

3. The method of claim 1 wherein the directing step includes maintaining a distance of about 0.5 to 10 centimeters.

4. The method of claim 1 wherein the producing step includes supplying the liquid to the transducer at a position which causes the liquid particles to be insonified.

5. The method of claim 1 wherein the directing step further comprises:

directing the particle spray onto a surface containing bateria to kill the bacteria.

6. The method of claim 5 wherein the surface is human tissue.

7. The method of claim 5 wherein the liquid comprises at least one of an antibiotic and an antiseptic.

8. The method of claim 5 wherein the surface comprises a human tissue and the step of directing the particle spray onto a surface of human tissue delivers a drug into the human tissue.

9. The method of claim 8 wherein the drug comprises an antibiotic.

10. A method of delivering a liquid drug to a tissue comprising:

producing a particle spray of liquid drug particles produced by contact of liquid drug with an ultrasonic transducer operating at a frequency of between about 16 and 200 kilohertz; and

directing the particle spray onto a surface of the tissue while maintaining the transducer at a distance of at least about 0.5 centimeters.

11. A method of killing bacteria on a surface comprising:

driving an ultrasonic transducer to produce low frequency ultrasonic radiation, the transducer having a tip with a free end surface directly exposed to a surrounding ambient environment;

directing a liquid to the free end surface of the transducer wherein an atomized particle spray of the liquid is created upon contact of the liquid with the free end surface of the transducer, the particles of the spray carrying the ultrasonic radiation imparted by the free end surface; and

orienting the particle spray directly onto a surface containing bacteria while maintaining a distance of separation between the surface to be sprayed and the free end surface of the transducer.

12. The method of claim 11 wherein the step of directing the liquid further comprises:

delivering the liquid first to a side surface of the transducer adjacent to the free end surface such that the liquid is pulled to the free end surface by a vacuum created by the ultrasonic radiation on the free end surface of the transducer tip.

13. The method of claim 11 wherein the step of directing liquid includes delivering the liquid without compression to the free end surface.

14. The method of claim 11 wherein the spray orienting step includes orienting the spray without air pressure after the spray is created at the free end surface.

15. The method of claim 11 wherein the step of driving an ultrasonic transducer further includes producing longitudinal ultrasonic waves having a frequency from about 16 to about 200 kilohertz.

16. The method of claim 15 wherein the frequency is about 20 to 40 kilohertz.

17. The method of claim 11 wherein the step of orienting the particle spray further includes maintaining a distance of separation of about 0.5 to 40 centimeters.

18. The method of claim 11 wherein the liquid is water.

19. The method of claim 11 wherein the liquid includes at least one of an antibiotic and an antiseptic.

20. The method of claim 11 wherein the driving step includes producing radiation having an intensity of about 1.5 W/cm^2 over the free end surface.

21. The method of claim 20 wherein the driving step includes producing longitudinal ultrasonic radiation waves having an amplitude of about 50 microns.

22. The method of claim 11 wherein the directing step further includes creating a particle size of the spray of about 3 to 10 microns.

23. A method of delivering a liquid drug into a tissue comprising:

driving an ultrasonic transducer to produce low frequency ultrasonic radiation, the transducer having a tip with a side surface and a free end surface directly exposed to a surrounding ambient environment;

directing a liquid drug to the side surface of the transducer adjacent to the free end surface such that the liquid drug is pulled to the free end surface by a vacuum created by the ultrasonic radiation being emitted from the free end surface of the transducer tip, wherein an atomized particle spray of the liquid drug is created upon contact of the liquid drug with the free end surface of the ultrasonic transducer, the particles of the spray carrying the ultrasonic radiation imparted by the free end surface; and

orienting the particle spray directly onto a surface of the tissue while maintaining a distance of separation between the tissue surface and the free end surface of the transducer.

24. A method of killing bacteria on a surface comprising:

driving an ultrasonic transducer to produce longitudinal ultrasonic waves having a frequency of about 16 to 200 kilohertz, the transducer having a tip with a side surface and a free end surface directly exposed to a surrounding ambient environment;

directing a liquid to a location on the side surface of the transducer tip adjacent to the free end surface such that the liquid is pulled to the free end surface by a vacuum created by the ultrasonic waves radiating from the free end surface of the transducer tip, wherein an atomized particle spray of the liquid is created upon contact of the liquid with the free end surface of the ultrasonic transducer, the particles of the spray carrying the ultrasonic waves radiating from the free end surface; and

orienting the particle spray directly onto the surface to be sprayed while maintaining a distance of separation between the surface to be treated and the free end surface of the transducer, wherein the distance of separation is about 0.5 to 10 centimeters.

25. The method of claim 24 wherein a distance between the location of the side surface and the free end surface depends on the frequency of ultrasonic radiation.

26. A method of killing bacteria on a surface comprising:

(a) directing onto the surface a particle spray of insonified liquid particles from a free end surface of an ultrasonic transducer operating a frequency of between about 16 and 200 kilohertz for a period of about 30 seconds; and

(b) repeating step (a) a plurality of times.

27. The method of claim 26 wherein the directing step further includes: maintaining a distance of separation between the free end surface and the surface to be sprayed of between about 0.5 and 10 centimeters.

28. The method of claim 26 wherein the repeating step includes repeating step (a) at spaced time intervals.

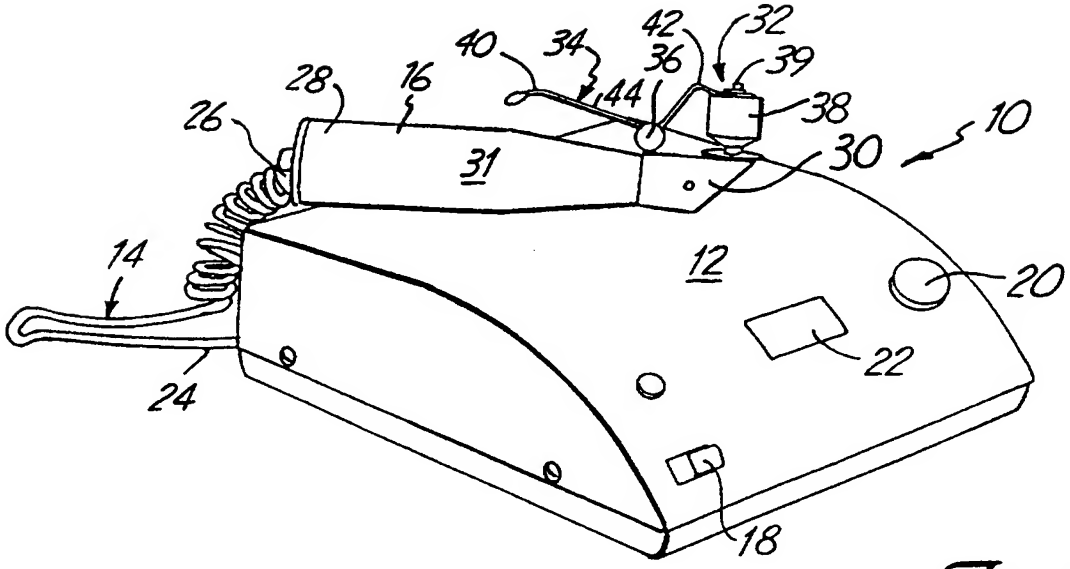


Fig. 1

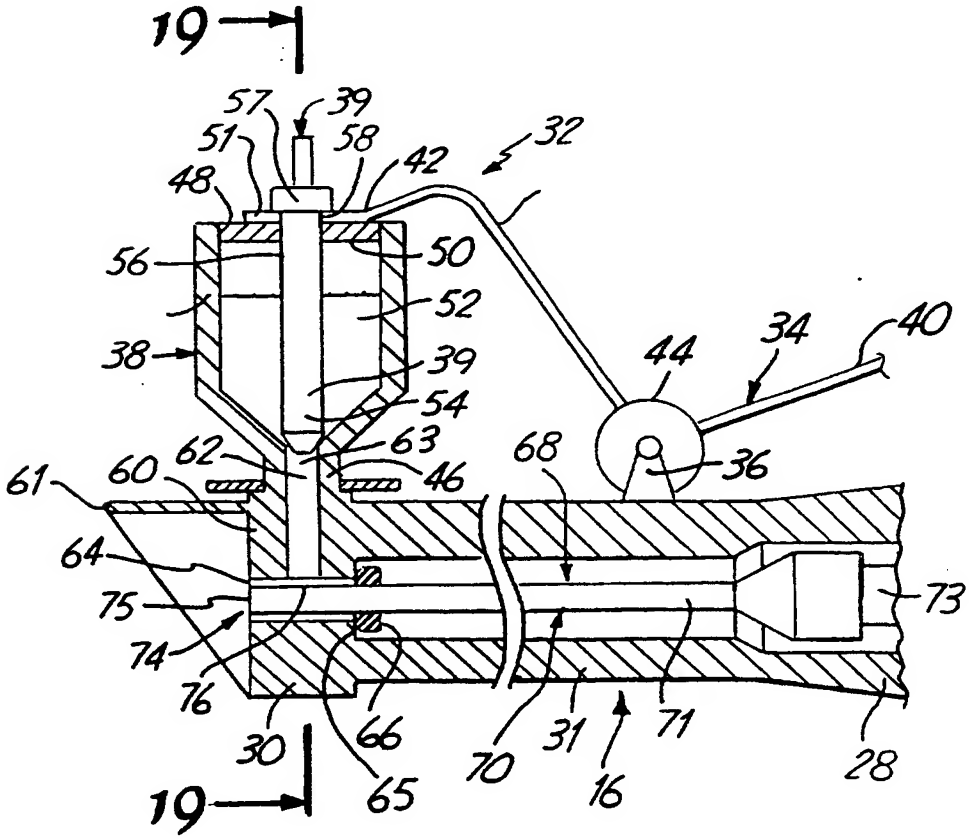
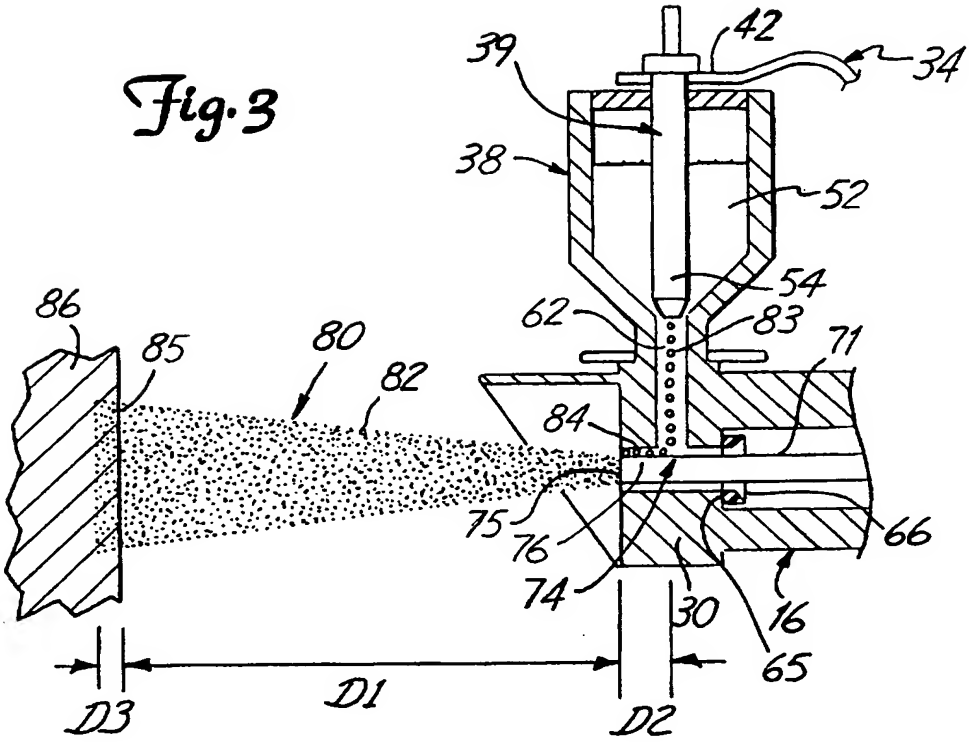


Fig. 2

Fig. 3



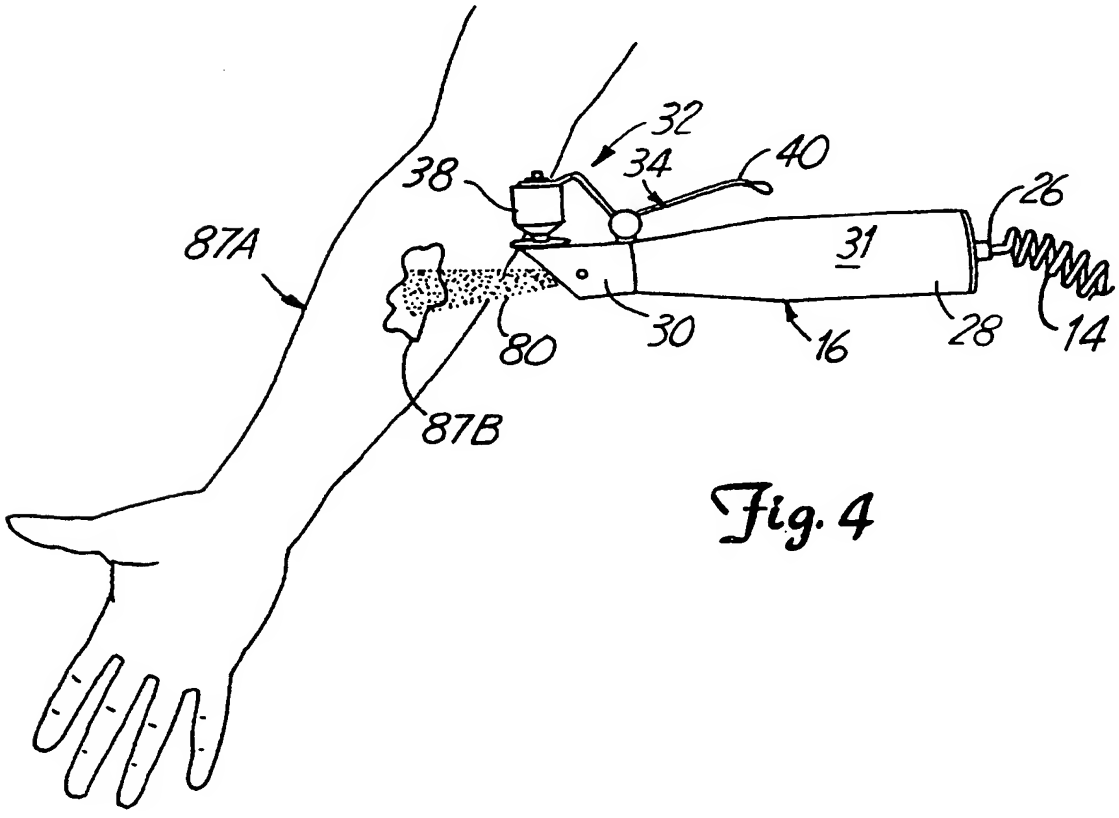
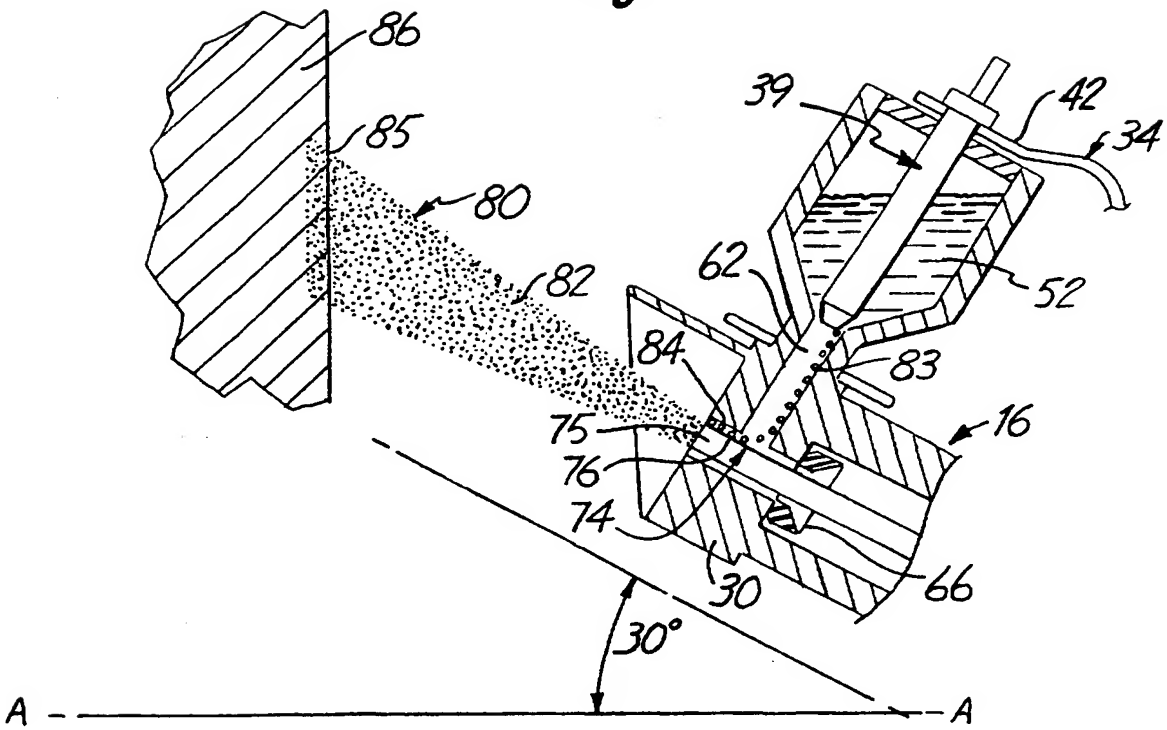
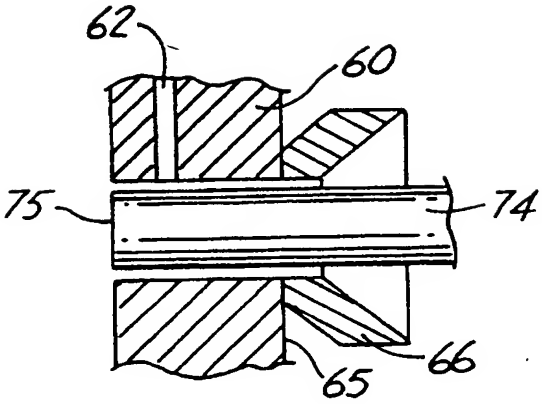


Fig. 4

Fig. 5





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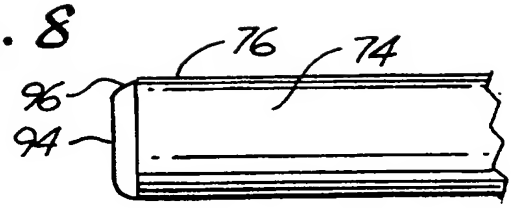

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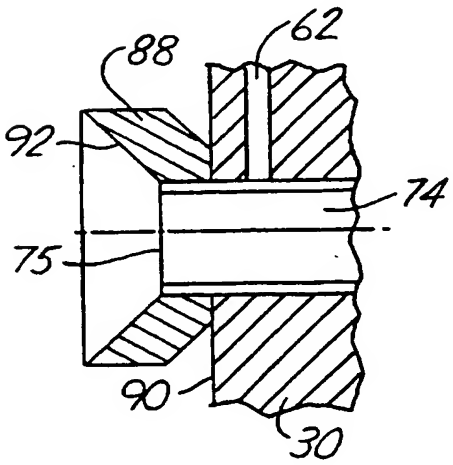


Fig. 7

Fig. 9

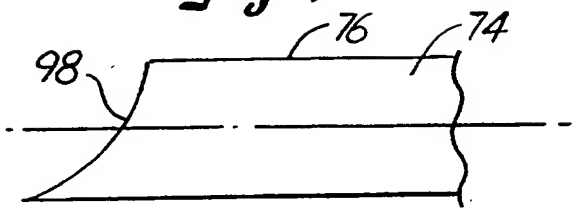


Fig. 10

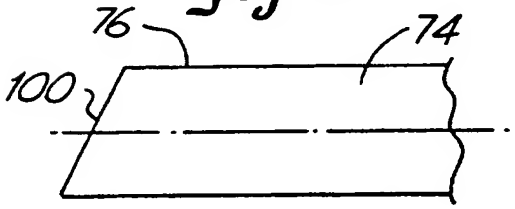


Fig. 11

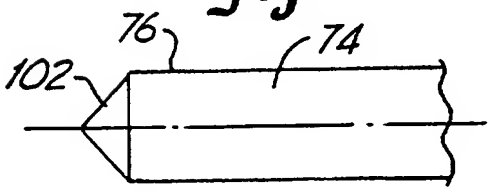


Fig. 12

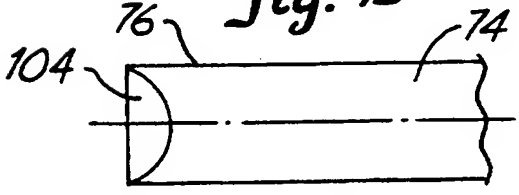


Fig. 13

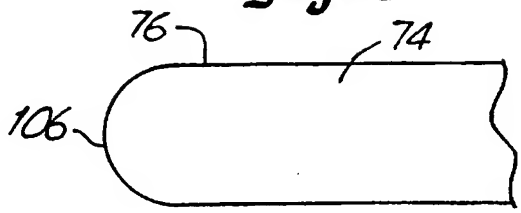
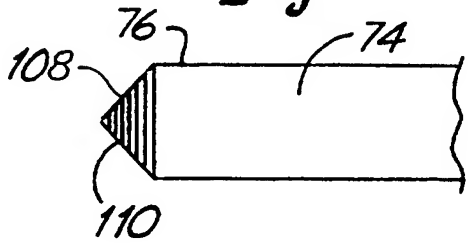


Fig. 14



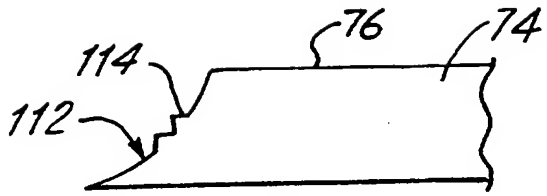
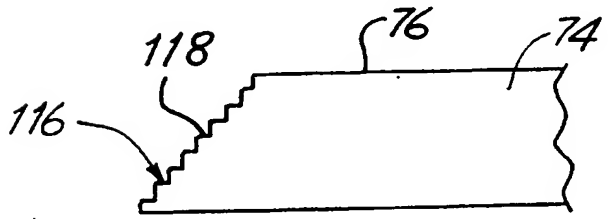


Fig. 15



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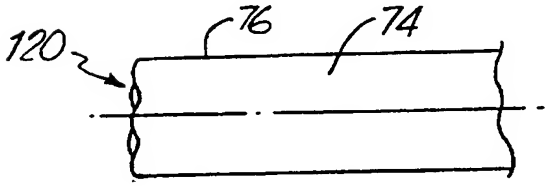

Fig. 17

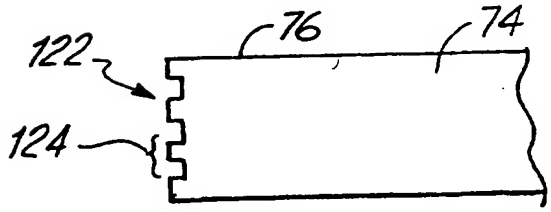

Fig. 18

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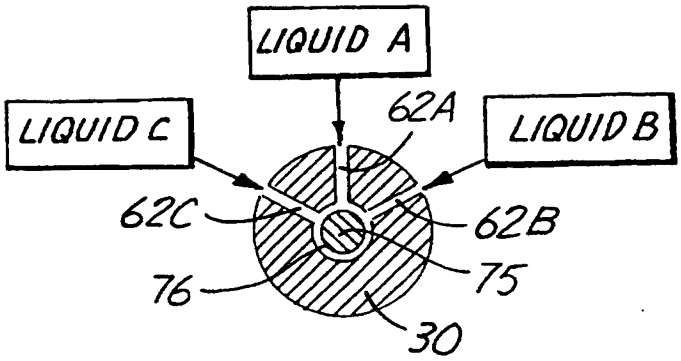

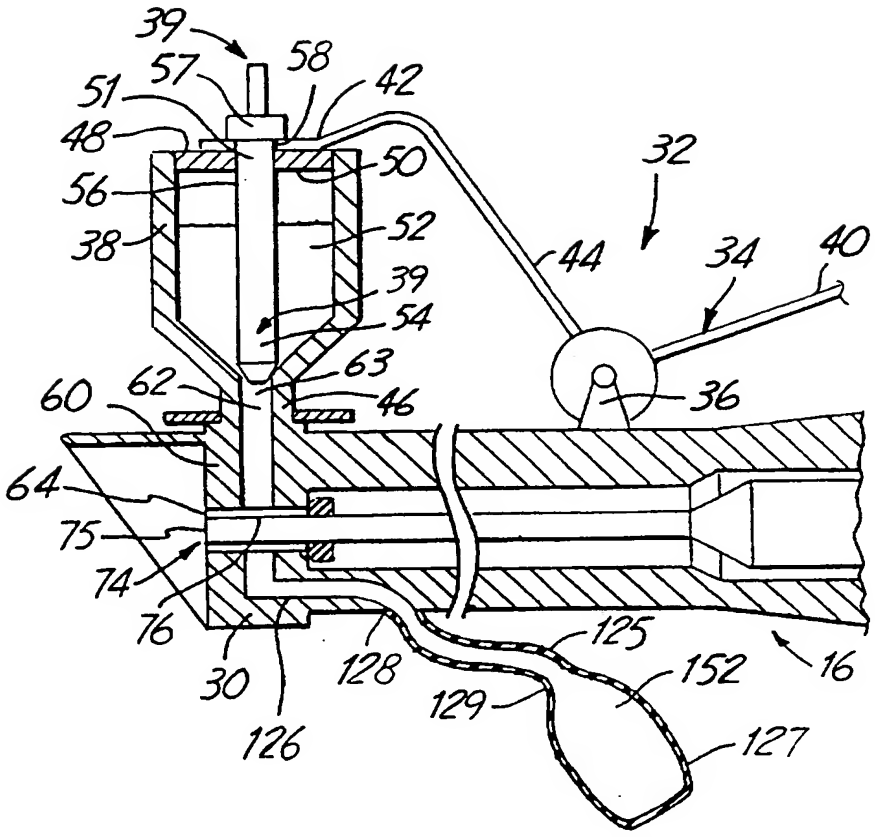
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Fig. 20

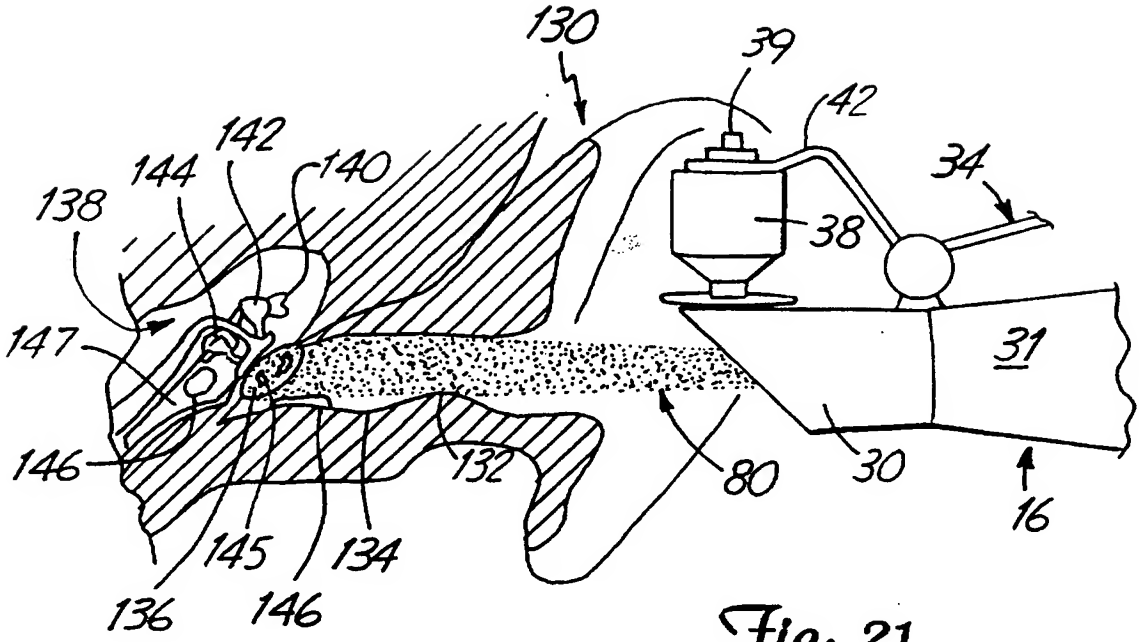

Fig. 21

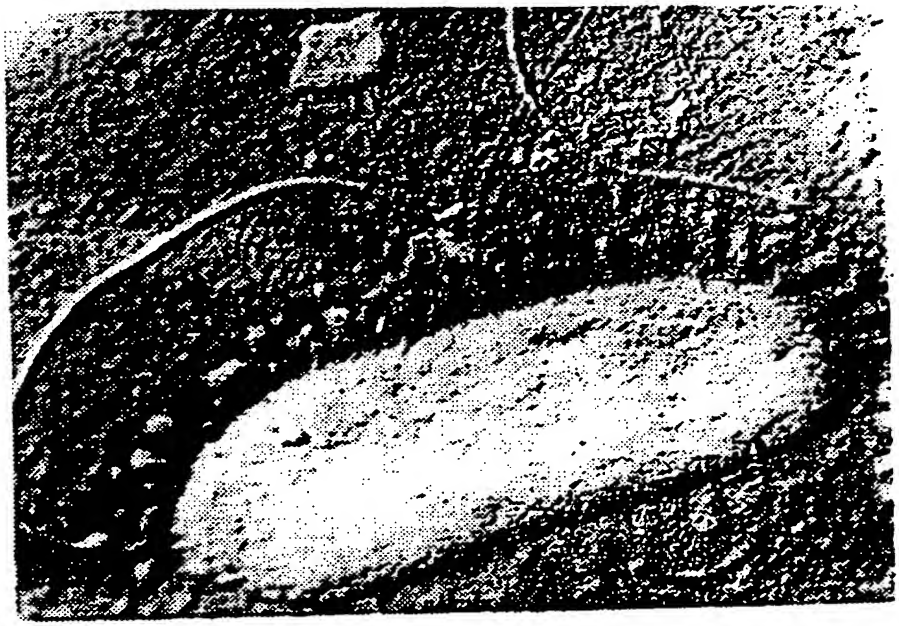

Fig. 22

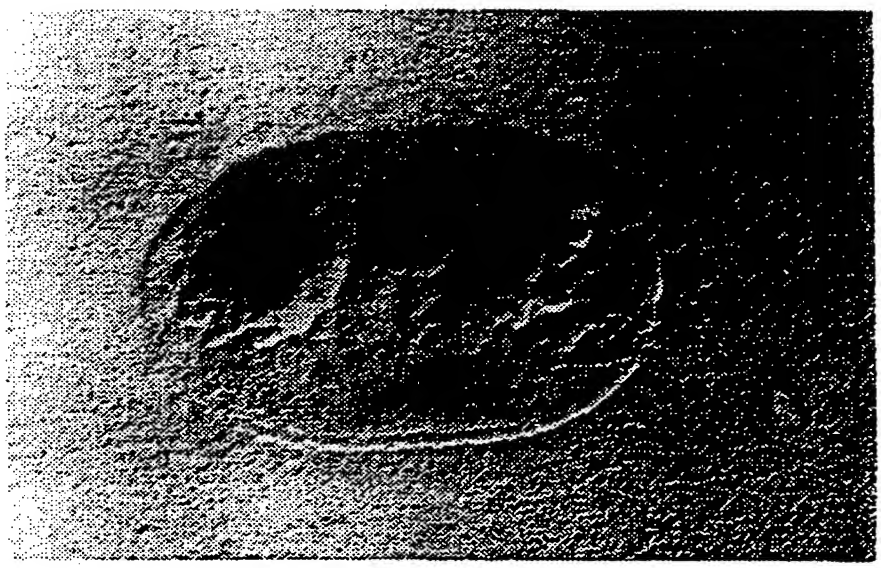

Fig. 23

Fig. 24

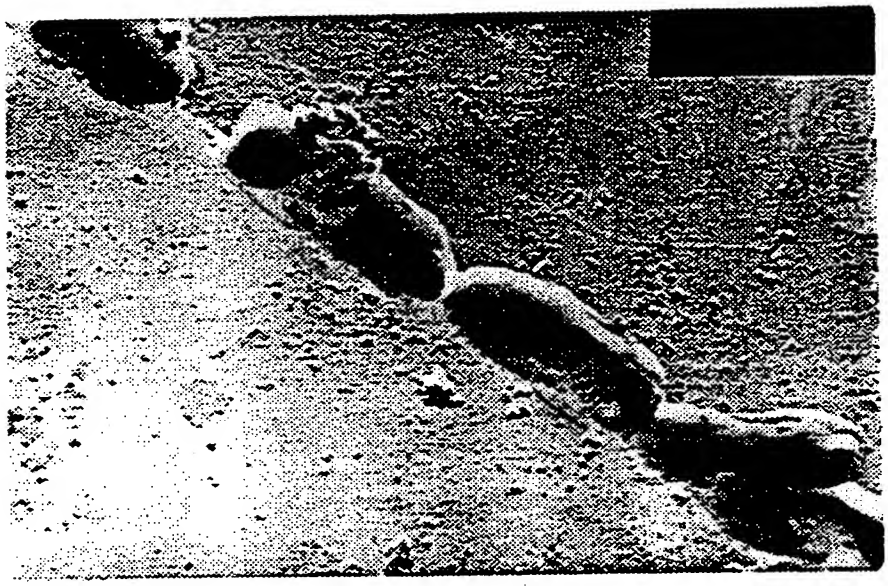

Fig. 25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/14926

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61H 1/02; A61M 11/00, 35/00; B05B 1/08, 3/04, 17/06
US CL :128/200.14, 200.16, 202.16; 239/102.2; 601/2; 604/289

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/200.14, 200.16, 202.16; 239/102.2; 601/2; 604/289

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 4,331,137 (SARUI) 25 May 1982, see entire doument.	1-28
Y	US, A, 4,551,139 (PLAAS ET AL.) 05 November 1985, see entire document.	1-28
Y	US, A, 3,874,372 ,(LE BON) 01 April 1975, see entire document.	1-28
Y	US, A, 5,076,266 ,(BABAEV) ,31 December 1991 see entire document.	2, 6-15, 21-23
Y	US, A, 4,767,402 (KOST ET AL.) 30 August 1988, see entire document.	16, 17
Y	US, A, 5,062,795 (WOOG) 05 November 1991, see entire document.	18

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
07 FEBRUARY 1996

Date of mailing of the international search report
27 FEB 1996

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